The ICF as a Framework for Post Burn Dysfunctioning: Evaluation, Quality of Life and Vacuum massage in Patients with Hypertrophic Burn Scars

Het ICF als referentiekader voor dysfunctioneren na brandwonden

Evaluatie, kwaliteit van leven en vacuum massage bij patiënten met hypertrofische brandwonden littekens

Faculty of Medicine and Health Care Sciences

Antwerp 2016

Dissertation submitted in fulfilment of the requirements for the degree of Doctor in Medical Science at the University of Antwerp to be defended by Jill Meirte

Proefschrift voorgelegd tot het behalen van de graad Doctor in de Medische Wetenschappen aan de Universiteit Antwerpen door Jill Meirte

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This book was made possible through contributions from Courage Khazaka HmbH, Cologne, Germany and Störz Medical AG Switzerland.

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LIST OF ABBREVIATIONS

ISBI: International Society for Burn Injuries
WHO: World Health Organisation
TBSA: Total Body Surface Area
FOD-SPF: Federal Public Service Health, Food Change Safety and Environment
ZNA: hospital Network Antwerp
TEWL: transepidermal water loss
ICF: International Classification of Functioning Disability and Health
OT: occupational therapist
PT: physical therapist
ICC: intra-class correlation coefficient
TPT: Touch Pressure Threshold
r: Pearson's correlation coefficient
MHz: megahertz
VSS: Vancouver Scar Scale
POSAS: Patient and Observer Scar Assessment Scale
r_s: Spearmans rho
HRQOL: health related quality of life
BSHS-B: Burn Specific Health Scale-Brief
α: alpha
M-index: melanin index
E-index: erythema index
RCT: randomised clinical trial
PROMs: patient reported outcome measures
SWMT: Semmes Weinstein monofilament test
GRRAS: guidelines for reporting reliability and agreement studies
SEM: Standard error of measurements
ADADAD: ascending descending ascending descending ascending descending
CI: confidence interval
SD: standard deviation
MD: mean difference
d: difference
SEM%: standard error of measurement expressed in percentage
EC: ethical commitee
EQ-5D: European Quality of Life 5 Dimensions
SF-36: Short Form-36 items
MESH: Medical Subjects Headings
SIP: Sickness Impact Profile
QLQ: Quality of Life Questionnaire
QOLS: Quality of Life Scale
DLQI: Dermatology Life Quality Index
LOS: length of stay
ECM: extra-cellular matrix
MCID: minimal clinically important difference
US: ultrasound
Mb: millibar
Hz: hertz
W: working time
R: resting time
'': seconds

VAC: vacuum-assisted closure
NPWT: negative pressure wound therapy

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GENERAL INTRODUCTION

'Wounds may heal but scars are forever'

The skin is the largest organ of our body. It does not only protects us from harm, but also gives us our unique expression. When the integrity of that skin is damaged, a regenerative process of wound healing is started, which not always leads to the complete disappearance of scars. In the event of prolonged or disturbed healing a pathological scar is formed with major functional and psychological consequences. A burn injury is a traumatic event followed by all kinds of interventions by different health care workers, starting in the acute phase and leading to long-term care and follow-up for the patients. Scars and in particular burn scars are the topic of this doctoral thesis. Treatment of the skin by physical therapists is a recent development, although we palpate our patients and always work with our hands directly on our patients' skin… Physical therapy for scars is a relatively new treatment modality, lacking knowledge amongst health practitioners and scientific research. The overall goal for every health care practitioner is to recover the patients to the pre-injury state and to strive for an optimal reintegration into society with unaltered potential. To do so we need to assess and treat our patients in the best possible (evidence based) way. Assessment of scars is important in the clinical follow-up of patients, for comparative evaluation of treatment modalities and for measuring the efficacy of our interventions. Possible assessment tools described in this thesis were in most cases not yet proven valid or reliable in scars or were not yet being used within this (burn) population. The interventions included in this thesis were being used clinically, although very little literature on the effects could be found. New assessment tools for scars keep emerging. Multiple treatment modalities primarily developed for other musculoskeletal or skin disorders find their way within the treatment of scars but are frequently lacking evidence for their efficacy. This doctoral thesis tries to fill some of the gaps still present in this fast developing domain of physical scar management.

WHAT IS A BURN INJURY

The International Society for Burn Injuries (ISBI) and the World Health Organisation (WHO) define burns or thermal injuries as: 'the distraction of some or all layers of cells forming the human skin, which is provoked by close contact with hot liquids, hot solids or flames resulting in scalds, contact burns and flame burns[1].' Burns and their severity can be classified in different ways and the most common are the classification by cause (e.g., scalds, flame, friction, chemical, electric), by degree of depth (first, second and third degree burns) and by the area of body surface area

burned (% Total Body Surface Area TBSA)[1]. The skin is the largest organ in the human body and is important for aesthetic appearance, but its most important functions are protection against pathogens and damage, regulation of fluid evaporation, sensation, thermoregulation and its role in the immune system[2]. An inevitable consequence of burns is (severe) scarring. Scars are areas of fibrous tissue that replace the normal skin after wound repair.

It is very hard to describe the incidence of burn injuries in Belgium, since no national burn registry has been implemented. It is estimated that yearly about 500-600 patients with severe burn injuries are treated in one of the 5 burn care centres that resort under the Federal Public Service Health, Food Change Safety and Environment (FOD –SPF). About 371 patients with severe burn injuries were treated in the Military Hospital in 2012 which resorts under the Ministry of defence[1].

These 6 acute burn care centres have a total of 70 beds. The burn centres are characterised by highly specialised multidisciplinary teams and focus on the acute phase, but also play a role in the aftercare process. Aftercare services vary between the burn centres in terms of intensity (frequency of outpatient visits), disciplines involved (multidisciplinary consultations with physiotherapy, orthopaedic technician, wound care nurse, psychologist,…) and duration of follow-up. Hospital Network Antwerp (ZNA) Stuivenberg uses a unique care model for organisation of aftercare for the majority of the patients by collaborating with Oscare, Organisation for Burns, Scar Aftercare and Research[1], an aftercare- and research centre for burns and scars. Focused on the aftercare in Oscare in 2014 844 patients were treated and 2251 medical consultations were performed, 4747 physical therapy sessions were given to 120 individual patients[3]. This thesis focusses on the physiotherapeutic aftercare for burn scars (after wound closure) and was made possible by a collaboration between the University of Antwerp and Oscare.

FORMATION OF A (BURN) SCAR

Repair of the skin starts within 24-72 hours after injury with an inflammatory reaction as a first step. The wound is cleaned by white blood cells and vasodilatation in the capillaries causing red colour and oedema in the skin[4,5]. In a second phase which may last for up to six weeks (the proliferation- or fibroplastic phase) epithelisation, wound contraction and collagen production occur, characterising the progress in time. Granulation tissue is formed and myofibroblasts (transdifferentiated fibroblasts) play a key role in contraction of the wound edges (closing the wound)[6]. The maturation or remodelling phase takes at least one year to complete and is the last

step in normal wound healing in which stronger collagen is produced and scar tissue is formed[4]. The different steps in normal wound healing are illustrated in Figure 0-1. The presence of myofibroblasts should decrease after wound closure but in hypertrophic scars the myofibroblasts persist[5]. Various factors like size of the wound, location, infection, age, skin type, health of the patient and mechanical tension may influence normal scar formation and cause hypertrophy[7,8]. Furthermore, wounds that are not healed within 2-3 weeks and have a prolonged or excessive inflammatory phase[9] are more likely to become hypertrophic scars[10]. Depending on the depth of the (burn) wounds spontaneous healing, partial thickness or full thickness skin grafts and other surgical treatment might follow. Scar maturation may last as long as two years[2] and besides the aesthetic consequences scars affect functions of the skin like sensation and the capacity to evaporate (due to the diminished sweat glands).

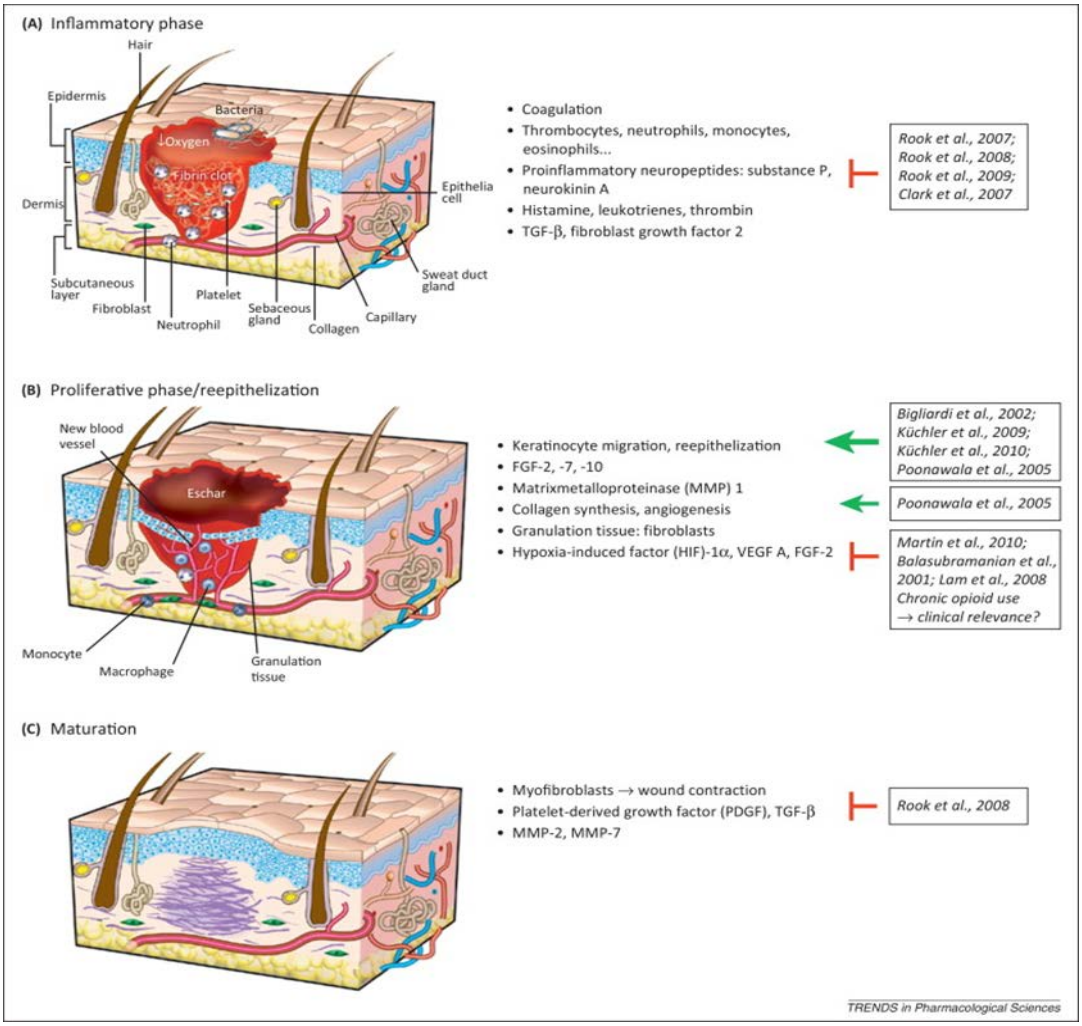

Figure 0-1 Illustration of the different phases in normal wound healing (Stein et al. 2013)

HYPERTROPHIC SCARS AND THEIR CHARACTERISTICS

Peacock defined a hypertrophic scar as a scar raised above the skin level that stays within the confines of the original lesion[11]. The incidence of hypertrophic scarring varies from 40% to 70% following surgery and from 30% up to 91% following burns[12–17]. Hypertrophic scars may have aesthetic and physical consequences. The red to purple coloured scar due to increase blood flow in the capillaries, may cause pain, itch, alteration in sensitivity and a decrease in range of motion due to skin inelasticity (because of the lack of elastin) especially if the scarred skin overlaps a joint. One year after a burn injury 35% of the patients experience pain[18] and after 2 years 67% of the patients still complain of pruritus[19]. The integration of patients with hypertrophic scars in our society which emphasis on external appearance may also cause problems[20].

Besides colour the most important physiological characteristics that provide information on the maturation of hypertrophic scars are transepidermal water loss (TEWL) and water content[21,22]. TEWL is an important parameter to evaluate skin barrier function and the efficiency of the skin to retain water. TEWL rates are usually higher in burn scars since the skin is disrupted and the stratum corneum barrier functions are damaged[20].

THE ICF FRAMEWORK AND FUNCTIONING IN BURN PATIENT EVALUATION

The International Classification of Functioning Disability and Health (ICF) is a worldwide used framework to describe a health condition of a patient in a broad bio-psycho-social context. The ICF was approved in 2001 by the WHO. It is now widely used, for instance to measure health status at population level, in clinical and epidemiological settings to classify functional status assessment at the individual level, and to identify goal settings, treatment planning and monitoring as well as outcome measurement[24]. The ICF describes different domains of dysfunctioning from body, individual and societal perspective. Its core structure consists of 2 parts (a) Functioning and Disability and (b) Contextual Factors. Within Functioning and Disability 2 subcategories are recognised; (1) Body and (2) Activities and Participation. Both Environmental and Personal Factors comprise the Contextual Factors category. The Body perspective is further divided into two categories. The first is Body Functions and lists all physiological functions of body systems. The second, Body Structures, lists all anatomical parts of the body. The individual and societal perspectives are elaborated in the domain Activities and Participation. The Contextual Factors (Environmental or Personal Factors) may affect (facilitate or inhibit) all components of functioning and disability. Environmental factors include the physical, social and attitudinal environment (e.g., profession, living environment, social

support) and Personal factors refer to one's attributes (e.g., age, gender, coping strategies) or internal influences on functioning[25].

Disability involves dysfunctioning at one or more of these levels: impairments in Body function or structures, Activity limitations and Participation restrictions. (Figure 0-2)

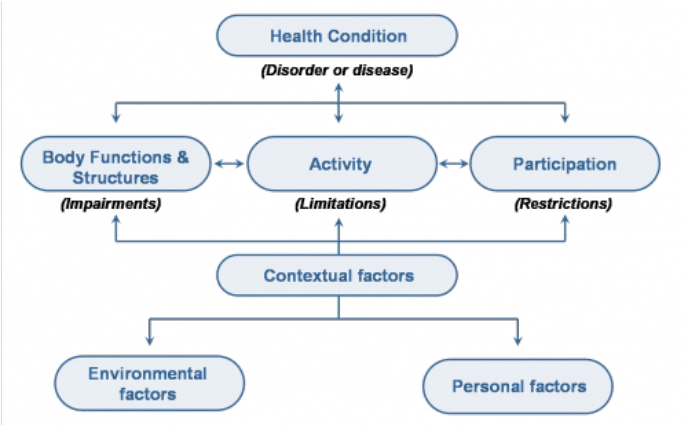

Figure 0-2 Illustration of the ICF framework by the World Health Organisation

Patients who suffer from burn injuries encounter devastating medical conditions and may be confronted with long-term impairments in Body structures (e.g., hypertrophic scars) and Body Functioning (e.g., pain, itch), Activity limitations (e.g., inability to write) and Participation restrictions (e.g., inability to go to school or work) during their rehabilitation. Despite the extensive use of the ICF in many other rehabilitation areas in medicine and the implementation within education programs of several health care educations (occupational therapist (OT), physical therapist (PT), nursing, medicine) the implementation and utilisation in clinical practice and research in the burn population remains low[26–28]. This doctoral thesis will focus on bridging the gap between the ICF and clinical practice, the latter comprising burn scar assessment and treatment. Dysfunctioning in patients with (burn) scars will be the main theme throughout this thesis. Exploration of outcome measures across all levels of the ICF may make the very complex consequences of a burn injury more comprehensible.

OBJECTIVE AND SUBJECTIVE SCAR ASSESSMENTS IN PATIENTS WITH SCARS.

Several quantitative and qualitative measurements are needed to quantify scars for the purposes of determining response to treatment and evaluating outcomes. Scar assessments can be objective or subjective. Objective assessments provide a quantitative measurement of the scar, whereas subjective assessments are observer dependent[29].

The **objective assessment** of scars can evaluate one or more aspects (impairments in Body Structures or Body Functions). Objective tools for scars and hypertrophic scars enable

comparison of different treatment protocols and allow an objective follow-up. Scar assessment tools enable objective and reproducible evaluation of scars. They are essential for scientific studies, for medico-legal purposes, and for the clinical follow-up of an individual patient[22]. Various scar characteristics and impairments in Body Structures and Body Functions can be measured with objective assessments. The focus of this doctoral thesis will be on the parameters pain, itch, colour, TEWL, touch pressure threshold and the measurement of epidermal and dermal density and thickness.

Evaluations of Impairments in Body Structures and Body Function

Colour and TEWL in burn scars

Several objective tools for colour measurement exist based on tristimulus reflectance colorimetry and narrow band spectrophotometry or both methods combined. Based on the first method the Minolta Chromameter (Konica Minolta, Japan) and the Skin Colorimeter (Courage Khazaka Electronic HmbH, Cologne, Germany)[30] are the most commonly used. Within narrow band spectrophotometry the Mexameter (Courage Khazaka Electronic HmbH, Cologne, Germany) has been described. The DSM II ColorMeter (Cortex Technology, Hadsund, Denmark) combines both methodologies. Clinimetric properties (validity and reliability) were evaluated on scars and the Mexameter, the Colorimeter and the DSM II ColorMeter provided reliable inter-rater colour data (intra-class correlation coefficient (ICC) ≥ 0.83) on scar tissue[31] as well as the Minolta Chromameter (ICC ≥ 0.72)[32]. For validity the highest correlations with the POSAS vascularisation scores were erythema (Mexameter) (Pearson's correlation coefficient r= 0.59); LAB2 (Colorimeter) (r= 0.69) and erythema (DSM II) (r= 0.66)[31].

For the assessment of TEWL, an important physiological characteristic to evaluate the efficiency of the skin barrier, the Dermalab TEWL probe (Cortex technology, Hadsund, Denmark) shows good reliability for scar tissue[33]. Good ICC values for both intra- (ICC ≥ 0.86) and inter-rater reliability (ICC ≥ 0.78) were found in burn scars[33]. The Tewameter (Courage and Khazaka Electronic GmbH, Cologne, Germany) is another TEWL assessment tool based on the open chamber technique. No scar assessment trials have been done with the Tewameter and it has not yet been proven reliable for burn scars. A new combination tool the Scarbase Duo (Courage and Khazaka Electronic GmbH, Cologne, Germany) combines both scar properties colour and TEWL in a small and affordable assessment tool. It was our aim to investigate validity and reliability of this device, which had not yet been evaluated in burn scars.

Touch pressure threshold

Several types of sensation that are perceived by the skin might be reduced after a burn injury[28,34]. To determine the patients' capacity to protect themselves from heat and pain (which is of utter importance especially in burn scar patients) an adequate sensory-related assessment tool is required. The Touch Pressure Threshold (TPT) or light touch can be assessed with the Semmes Weinstein monofilaments[28]. Assessing TPT in burn scars allows us to determine how much the loss of sensation is compared to normal skin and also allows to evaluate even slight improvement in touch pressure threshold. The reliability of this assessment tool has not yet been investigated on burn scars.

Skin thickness and density

The change in scar thickness, particularly measured with ultrasound tools, has been adopted as one of the objective indicators for assessing the maturation of hypertrophic scars[35]. Ultrasound imaging is a non-invasive reliable and convenient method to visualise epidermal and dermal thickness and density. The DUB®Cutis (Taberna pro medicum, Lueneburg, Germany) a 22 megahertz (MHz) high frequency ultrasound tool has already been proven reliable for measuring dermal thickness and density of burn scars. For dermal thickness good ICC values for intra- (ICC ≥ 0.991) and interrater reliability (ICC ≥ 0.991) were found. For repeated measures of dermal density good intra- (ICC ≥ 0.967) and interrater (ICC ≥ 0.876) reliability was demonstrated[36]. The effects of treatments and maturation of scars can be monitored with this type of device[35]. Until now only the effects of compression therapy on mean scar thickness have been investigated in patients with hypertrophic scars[37].

Besides objective scar assessments subjective scar scales and Patient Reported Outcome Measures are important and show the impact of the scar and the different treatments on areas of health and functioning that are important to the person with scars.

Concerning **subjective** scar scales exist, the Vancouver Scar Scale (VSS) and the Patient and Observer Scar Assessment Scale (POSAS) are most frequently used in scar assessment studies[38,39]. The POSAS (see Appendix) has the added benefit of capturing patient ratings in comparison to the Vancouver Scar Scale and was proven more reliable than the latter[21,40]. Inter-rater reliability for the POSAS total score was acceptable (ICC= 0.92 for 4 raters, ICC= 0.73 for 1 rater). Convergent validity with the VSS was high (Spearmans rho (r_s)= 0.89, $p< 0.001$)[21]. The POSAS includes subjective ratings for pain, itch, colour, stiffness, thickness and relief (all impairments in BS or BF) with the Patient Scar Assessment Scale. The observer rates vascularity, pigmentation thickness, relief, pliability and surface area with the Observer Scar Assessment Scale. The POSAS is a reliable and valid scale to measure scar quality[41].

HEALTH RELATED QUALITY OF LIFE (HRQOL) IN PATIENTS WITH BURN SCARS

'Scars you can't see are the hardest to heal'

The main goal of HRQOL measures is to describe the burden of disease of the population studied. HRQOL instruments focus on activities and participation, which are considered to be the components most relevant to patients and society, and are applicable to all health conditions. These instruments make it possible to compare functioning and health across health conditions, populations, and interventions[42]. The most commonly used tool for quantifying HRQOL and thus quality of recovery in adult patients with burns is the Burn Specific Health Scale (BSHS)[43]. The Burn Specific Health Scale Brief (BSHS-B) (see Appendix) was created to abbreviate the initial 80 item BSHS to a 40-item questionnaire and proved to have validity (strong correlation with the BSHS r= 0.86 and with the BSHS Revised r=0.98) and reliability (high internal consistency Cronbach's α ranging from 0.75-0.93) in the burn population[44,45]. By its nature this population-specific measure lacks the normative values for healthy individuals and other patient populations[43]. Generic HRQOL measures address these shortcomings. Administering both generic and burn specific measures can provide a more detailed profile of the HRQOL impacts of burn scars.

Health-care interventions are intended to restore impairments in Body Structures and Body Functions, to overcome Activity limitations and Participation restrictions, and to prevent the development of new symptoms and disabilities[42]. It remains unclear which generic HRQOL questionnaires are used within the burn population and to what extent these cover the domains of the ICF.

CLINIMETRIC PROPERTIES OF THE MEASURES INVESTIGATED IN CHAPTER 2-6 OF THIS THESIS

Table 0-1 summarises the current status about the clinimetric properties of the outcome measures in Chapter 2-6 of this thesis.

Table 0-1 Clinimetric properties of the outcome measures in this thesis

	Measure	Reliability	Validity
Colour	**Mexameter**	intraICC$_{scar}$ Melanin index ≥ 0.89[46] intraICC$_{scar}$ Erythema index ≥ 0.74[46] intraICC$_{healthy\ skin}$ M-index ≥ 0.94[46] intraICC$_{healthy\ skin}$ E-index ≥ 0.82[46] interICC$_{scar}$ M-index ≥ 0.95[47] interICC$_{scar}$ E-index ≥ 0.82[47] interICC$_{healthy\ skin}$ M-index ≥ 0.99[47] interICC$_{healthy\ skin}$ E-index ≥ 0.97[47] interICC E-index$_{scar}$ 0.90 $_{healthy\ skin}$ 0.92[31] interICC M-index$_{scar}$ 0.97 $_{healthy\ skin}$ 0.94[31]	Mexameter E-index with POSAS vascularisation Pearson's r= 0.59[31] Mexameter M-index with POSAS pigmentation Pearson's r= 0.75[31]
TEWL	**Tewameter**	Unknown; addressed in Chapter 2	Unkown; addressed in Chapter 2
TPT	**Semmes Weinstein aesthesiometer**	Unknown; addressed in Chapter 1	Unknown; not addressed in this thesis
Dermal Thickness/ Density	**DubCutis Ultrasound Scanner**	intraICC$_{dermal\ thickness}$ 0.99[36] interICC$_{dermal\ thickness}$ 0.99[36] intraICC$_{dermal\ density}$ 0.97[36] interICC$_{dermal\ density}$ 0.88[36]	Unknown; not addressed in this thesis
HRQOL	**BSHS-B** **Generic HRQOL measures**	internal reliability Chronbach's α= 0.75-0.93[45]	correlation with BSHS r= 0.86[45] after establishing which generic measures are most frequently reported (Chapter 3) these will be addressed in the discussion

This leads us to the following research questions in Part 1 of this thesis:

- What is the reliability of the Semmes Weinstein monofilament test within burn scars and healthy controls using the ascending descending procedure?

- What is the intra- and interrater reliability, validity and feasibility of the Scarbase Duo® for use in research and clinical application in burn scars?

- What are the most frequently used HRQOL measures used in burn rehabilitation? Are they able to describe the broad spectrum of dysfunctioning and the different domains of the ICF framework? What aspects do they measure and what is left uncovered?

- What is the convergence and discriminant validity between HRQOL measures in burn populations?

These questions will be addressed in Part 1 of the thesis 'Quality of Burn Measures' (Chapters 1 to 4).

PHYSICAL TREATMENTS FOR HYPERTROPHIC SCARS

The physical treatments for hypertrophic scars will be addressed in Part 2 of this thesis. Physical therapy plays a crucial role in the multidisciplinary approach of patients with burn scars during the acute and rehabilitation phase and includes multiple treatment methods like early mobilisation, splinting, cardiopulmonary training, exercise therapy and also scar management[23]. Physical scar management -including manual and mechanical skin techniques- are currently being used clinically in physiotherapeutic treatments, although evidence based guidelines (based on good quality randomised clinical trials (RCT)) on physiotherapeutic skin treatments are lacking. A recent review on the effects of conservative treatments of burn injuries found twenty-two randomised and controlled clinical trials. This systematic literature search concluded that pressure therapy and silicone therapy are evidence based treatments for hypertrophic scar formation with improvements of scar thickness, redness and pliability[48].

Pain and pruritus significantly improve with massage therapy and also objective measures on thickness, melanin, erythema, TEWL and elasticity showed promising results for massage therapy[23,49]. Massage therapy shows positive effects on patient's perspectives and scar characteristics[23] although limited proof exists. The few studies that have been written had small sample sizes, used sometimes only subjective measures and no clear explanation of the exact massage therapy, timing and or frequency was described[23].

Vacuum massage (or depressomassage or endermology) is a non-invasive mechanical massage technique. The treatment head of the machine creates a skin fold (with negative pressure or suction) that can be manipulated[50]. Although the vacuum massage was invented to treat traumatic burns[51], few studies on its effects on burn scars can be found. A recent review on the physiological effects of vacuum massage found evidence of collagen restructuring and remodelling[52], however the studies included in the review were of poor methodologic quality, not performed in humans or not performed on (burn) scars. It remains to be proven whether the described physiological efficacy of vacuum massage can be seen in burn scars. A recent comparative study found limited evidence on the improvement of colour and TEWL for vacuum massage therapy as an addition to standard of care (hydration, pressure garment, silicone and physical therapy)[23]. The effects of vacuum massage on pain, itch and diminished sensation (which are frequently reported impairments in functioning) were not yet explored in the burn population.

Mechanotherapy

Our body is constantly subjected to mechanical forces that directly affect cellular function, for instance the effect of gravity on mineral deposition in our bone tissue[53]. Studying these

mechanical forces is a growing interest amongst medical researchers. Mechanotherapy or the employment of mechanical means for the cure of disease has had several definitions and involves the physical therapy (e.g., massage therapy and orthopaedic rehabilitation)[53]. It is proposed that physical therapy helps in healing or homeostasis of tissue outside the musculoskeletal system and may be able to oppose against specific pathophysiology and diseases. Recently, mechanotherapy has been redefined as a therapeutic intervention that reduces and reverses injury to damaged tissue or promote the homeostasis of healthy tissue by mechanical means at the molecular, cellular or tissue level[53].

Since physical therapy involves non-invasive techniques and also non-invasive assessments, the idea was proposed to visualise the effects of vacuum massage on Body Structures. More specifically the effects on epidermal and dermal thickness and density was the topic of our interest. Investigating the short-term effects of vacuum massage measured with high-frequency ultrasound might reveal proof for collagen realignment[54].

All skin techniques (manual and mechanical) techniques like manual defibrosing massage techniques, shockwave therapy and vacuum massage work on that same principle of mechanotherapy with the aim to restructure the collagen network in the scar tissue and to reduce the impairments in body structures (thick, red scar) and impairments in functioning (e.g., inelastic, itchy, painful scar).

Standard of care

Pressure garments and silicone therapy are the most widely known evidence based conservative treatments for hypertrophic scars after a burn injury[55,56]. These treatment modalities are recommended in the European Burn Association Practice Guidelines[57], are part of recent scar management recommendations[58] and are considered as standard of care in the physical treatments of hypertrophic scars at Oscare. Both pressure and silicone therapy are subsequently included in the usual care treatment mentioned in the chapters of this thesis. The in-depth investigation of these treatments is beyond the scope of this doctoral thesis.

This leads us toward the research questions in Part 2 of this thesis: ‘Vacuum Massage’:

- What is the effect of vacuum massage on pain, itch and touch pressure threshold in burn scars?
- What are the short-term effects of vacuum massage on epidermal and dermal density and thickness in burn scars?

These aspects will be addressed in Chapters 5 and 6.

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Part 1
Quality of burn measures

In this Part 1 the quality of both subjective patient-reported outcome measures (PROMs) and objective measurements for burn scars will be addressed. Four chapters are included. The first chapter elaborates on the reliability of an objective tool to assess the touch pressure threshold in burn scars. Chapter 2 is a study investigating both reliability and validity of a dual assessment tool to measure TEWL and colour. In Chapter 3 the HRQOL used in the burn population are being compared against the ICF framework while Chapter 4 focusses on the convergent and discriminant validity of those HRQOL measures.

1 INTERRATER AND INTRARATER RELIABILITY OF THE SEMMES WEINSTEIN AESTHESIOMETER TO ASSESS TOUCH PERCEPTION THRESHOLD

Published as:

Meirte J, Moortgat P, Truijen S, Maertens K, Lafaire C, De Cuyper L, Hubens G, Van Daele U. Interrater and intrarater reliability of the Semmes Weinstein aesthesiometer to assess touch pressure threshold in burn scars. Burns 2015;41:1261-7. doi:10.1016/j.burns.2015.01.003.

Abstract

Burn scars are frequently accompanied with sensory deficits often remaining present months or even years after injury. Clinimetric properties of assessment tools remain understudied within burn literature. Tactile sense of touch can be examined with the touch pressure threshold (TPT) method using the Semmes Weinstein monofilament test (SWMT). There is in recent research no consensus on the exact measurement procedure when using the SWMT.

The aim of this paper was to determine the interrater and intrarater reliability of TPT within burn scars and healthy controls using the 'ascending descending' measurement procedure. We used the newly developed guidelines for reporting reliability and agreement studies (GRRAS) as a basis to report this reliability study. In total 36 individuals were tested; a healthy control group and a scar group.

The interrater reliability was excellent in the scar group (ICC= 0.908/SEM= 0.21) and fair to good in the control group (ICC= 0.731/SEM= 0.12). In the scar group intrarater ICC value was excellent (ICC= 0.822/SEM= 0.33). Within the control group also an excellent intrarater reliability (ICC= 0.807/SEM= 0.27) was found.

In conclusion this study shows that the SWMT with the 'ascending descending' measurement procedure is a feasible and reliable objective measure to evaluate TPT in (older) upper extremities burn scars as well as in healthy skin.

1.1 INTRODUCTION

Burn scars are frequently accompanied with sensory deficits like pain, pruritus and hyposensibility, often remaining present months or even years after injury[1–3]. The prevalence of paresthetic sensation was found above 70% in patients 1 year or more after burn[1]. The modalities of touch, two-point discrimination, warming and vibration are all significantly reduced after burn[4]. The underlying pathophysiology of these impairments in body functions is unclear[5,6]. Destruction of nerve fibres or nerve receptors, surgical interventions (e.g., skin grafting) and hypertrophic scarring may contribute to the loss of sensation in healed burn scars[3]. Besides local anatomical changes, modifications in the central nervous system may play a role in the diminished sensation after burn[5].

Objective as well as subjective outcome measures are available to evaluate scars during rehabilitation. Pain, pruritus and typical scar characteristics (e.g., colour, thickness, etc.) in burn patients can be subjectively assessed with different scar scales (e.g., patient and observer scar assessment scale, Vancouver scar scale) and psychometric values have been fully documented[7–10]. Diminished sensibility can be measured objectively. However, sensory changes do not appear to have been routinely measured as outcomes in burns patients, which is surprising since sensation has been included as one of the core domains for burns outcome assessments[11]. The assessment of sensibility has been investigated since the 1960s but clinimetric properties of assessment tools remain understudied in burn literature[11] and predominantly focussed on correlation between sensation and anatomical properties of (grafted) skin[5,6,12,13]. Testing tactile sensibility can include pressure perception, two point discrimination, point localisation, vibration, etc.[14]. Tactile sense of touch can be examined with the touch pressure threshold (TPT) method. Pressure perception is relatively constant with ageing and changes between gender seems negligible[14]. Cutaneous pressure is received by the Merkel and Meissner mechanoreceptors present near the surface of the skin (epidermis/dermis). The Semmes Weinstein monofilament test (SWMT) is the most popular method for assessing TPT[5,14,15].

The SWMT is available in different kits. The mini-kit (with five monofilaments) is considered the minimum for screening normal versus abnormal sensory status. The SW complete kit, consisting of 20 sequentially graded thickness monofilaments is used to accurately categorise loss of function and to detect first signs of recovery[14].

Recent research lacks consensus on the exact measurement procedure when using the SWMT[15]. The 'forced choice' single staircase procedure was described in a reliability study in which 24 plantar halluces of 24 healthy subjects were assessed. In this study forced choice trials were used that consisted of the presentation of a stimulus and a blank in random order. The test session began

with the presentation of the monofilament that induced a pressure of 4.5 g/mm^2, followed by or preceded by a blank. If out of the five successive stimuli an incorrect response occurred from the participant, the next trial was presented with a more stiff monofilament two steps higher. This process was continued until five successive correct responses were made, which they then defined as the first staircase reversal. If five correct responses were obtained at the initial 4.5 g/mm^2, the next lower stimulus was presented in a similar fashion. Once the first staircase reversal was determined, either the 'two-down one-up' rule (2D) or the 'three-down one-up' rule (3D) was tested. In the 2D procedure, correct stimulus detection was required on two successive trials (each trial consisted of the presentation of a stimulus and a blank in random order) before the next lower pressure was presented. In the 3D procedure, three correct successive trials were required. In both instances, a single miss resulted in the presentation of the next stronger monofilament. A threshold was defined as the mean of all the stimulus levels at which a reversal occurred in the included reversal pairs. The 3D rule and the 2D rule as described by Tracey et al.[15] were compared and with four reversal pairs the 3D approach appeared more reliable ($r > .90$). The 'yes no' procedure and also the 'forced choice' were described in a review by Mueller et al. in a diabetic population. The 'yes-no' procedure instructs the patient to say ''yes'' each time the application of a SW monofilament is felt. Five to ten trials are taken at each site and the patient needs to respond to 80% of the trials to be graded a given value at that site, if not the patient is tested with the next higher monofilament[16]. In the 'forced choice' procedure the SW monofilament is applied during one of the two intervals (in the count of either ''one'' or ''two''). The patient is then asked whether they felt any sensation after the first or second interval. Weinstein introduced the average of an 'ascending descending' procedure to determine the TPT[14]. In a study on tactile, thermal and pain sensibility in burned patients the 'ascending descending' procedure was used to determine TPT in 121 subjects with upper limb scars 18 months after burn[5]. Likewise, in another burn study, in which 15 patients with grafted skin (10 months after grafting) were tested to evaluate TPT, this 'ascending descending' procedure was described[6]. Besides in the burn population, this 'ascending descending' procedure was also used in patients with chronic neuropathic pain[17,18]. This 'ascending descending' procedure is clinically being used to measure TPT in after burn evaluations in Oscare, an aftercare and research centre for burns and scars in Belgium, hence this procedure was chosen to evaluate in this study.

The clinimetric properties of the SWMT have been evaluated and quantified in other populations[5,19], there is however limited evidence on reliability of the different procedures within burns. The aim of this paper was to determine the interrater and intrarater reliability of the SWMT within burn scars and healthy controls using the 'ascending descending' procedure to evaluate TPT as described by various authors[5,6,15,17,18,20]. We used the newly developed guidelines for reporting

reliability and agreement studies (GRRAS) as a basis to report this reliability study[21]. This study is part of a larger comprehensive study in which the effects of physical treatment modalities in burn scars are being examined.

1.2 METHODS

1.2.1 Subjects

A convenient sample (a sample drawn without any underlying probability-based selection method) of burn patients were recruited at Oscare, Organisation for Burns, Scar Aftercare and Research, situated in Antwerp, Belgium. The start of enrolment was November 2012 and the completion date was the 1st of March 2013. This study focused exclusively on burn scars in the upper extremities, hands excluded. To verify the eligibility, the burn patients and control subjects were contacted by phone and invited to the aftercare centre. Inclusion criteria were: patients aged between 18 and 70 years, burn scars on the upper extremities, resulting from second or third degree burns, Caucasian skin type, 3 months or more after discharge from the burn unit. Exclusion criteria were as follows: scars only on the hands or other than upper extremities, patients with disorders affecting sensory function (e.g., diabetes, neurological diseases).

All participants signed informed consent and the protocol was approved by the ethics committee (MEC: 009; OG 031 Ethics committee of ZNA Antwerp E.C. approval no 4130).

1.2.2 Material

The Semmes-Weinstein aesthesiometer set (Rolyan Mono- filaments, Trademark of Smith & Nephew-copyright 1998) was used for the procedure, since this set can be used to measure recovery of sensibility[14]. This hand held tool consists of a series of 20 flexible calibrated nylon monofilaments of equal length and varying diameters (0.06–1.14 mm). Each of the 20 filaments is assigned a calibration value corresponding to the log of 10 times the strength required to bend the filament in demi-circle[22,23]. The pressure varies between 0.045 g/mm^2 and 447 g/mm^2 (representing the pressure given by the monofilaments with dimensionless values 1.65–6.65, respectively). The higher the value on the monofilament the more rigid and more difficult it is to bend. By design each filament exerts a specific pressure. Since all filaments bend when the specific pressure is reached, the amount of pressure presented at a given point is a function of the test instrument and not the examiner[24].

1.2.3 Procedure

The interrater and intrarater reliability was independently examined by two researchers; randomly selected from a pool of researchers and trained according to a pre-defined training protocol. Each researcher performed their measurements separately.

The participants were asked to lie down in a comfortable position supine or prone (depending on the volar or dorsal area to be tested). Participants were asked to close their eyes and to turn their head to the contralateral side. A permanent marker was used to mark the exact spot to test and a picture was taken to establish the location when a retest was done. The measurement location was the same in both groups meaning that every site of the burn patient was matched with the same site in the control subject. Healthy controls were chosen since many patients had bilateral scarring. Environmental factors were reduced to a minimum to keep attention high. Thus all tests were performed in a treatment room with controlled temperature and humidity (temperature: 21-23 °C and relative humidity: 40-60%) with the door closed. Participants stayed in this room and in the same position during the entire test procedure, while the raters separately went in and out of the room.

Before performing the tests and between the tests the patients received instructions on the test procedure. Participants were asked to say ‘‘yes’’ if a touch was felt. The filament was held vertically above the test area and slowly descended, the actual nylon filament was applied to the skin surface perpendicular to the length of the filament until it bowed (this in about 1.5 s), this bow was maintained once per monofilament for approximately 1.5 s (and removed in 1.5 s)[25]. Measurements were started with the 5.88 monofilament in both groups[18]. As shown in Figure 1-1a for the orientation series, measurements started at the 5.88 monofilament, if felt by the participant subsequently the monofilament three steps lower was applied (repeating the next step every time three monofilaments lower) until no perception could be felt. The filament last felt constituted the orientation value[5].

Subsequently six measurements were performed. The ascending series were started three filaments below the orientation value and three filaments above for the descending series (view Fig. 1-1a and b). All filaments in this range were successively applied for 1.5 s[26] until the subject reported its presence (ascending series) or absence (descending series). Time between stimulus application varied from 5 to 15 s to avoid temporal summation[27].

These steps were repeated three times resulting in an ‘‘ascending descending ascending descending ascending descending’’ (ADADAD) series. The threshold was calculated by the mean of the 6 values and considered as the TPT.

For the threshold the labelled units as displayed on the Semmes Weinstein monofilaments were used, not the values converted into grams. The total duration of the tests was about 30 min. The data of both assessors were compared to determine interrater reliability. The two measurements of the first assessor were used to investigate intrarater reliability. The two assessors performed their assessments at the same day with a period of rest in between to reduce fatigue. The reevaluation took place on average 12 days (range: 9-16 days, SD: 2.36 days) later in the burn group and 9 days (range: 7-13 days, SD: 2.14 days) in the control group, depending on the availability of the participants.

1.2.4 Statistics

Statistical analysis was performed using the SPSS 20 software package for Windows. The interrater and intrarater reliability were based on the measurements of two observers.

The intra-class correlation coefficient (ICC) with its 95% confidence interval (CI) was calculated to assess the interrater reliability for two observers and the intrarater reliability of one observer. The two-way- random effect model was selected and calculated for absolute agreement of the scores. Fleiss and Shrout classification for reliability coefficients (ICC2,1) was used to describe the degree of reliability[28]. The single measure ICC was used to interpret the results. In the results section the ICC findings are reported based on Rosner[29]. Specifically, an ICC value of less than 0.4 indicates poor reliability while an ICC between 0.4 and 0.75 indicates fair to good reliability. Lastly, an ICC over 0.75 indicates excellent reliability[29] .

To objectively identify reliability it is suggested to combine ICC (which represents a relative measure of reliability) with the standard error of measurements (SEM), which is the standard deviation (SD) of the difference between mean scores at baseline and follow-up (d) divided by the square root of two ($SEM = SDd/\sqrt{2}$). This quantifies the variability of the difference scores and is referred to as the typical error of differences[28] and the SEM percent change (SEM%). The SEM% was defined as $(SEM/\overline{x}) \times 100$, where $\overline{x}$ is the mean for all observations from test session 1 and 2.

The SEM estimates the measurement error across repeated measurements for a group of individuals, while the SEM% indicates measurement error independent of the units of measurement[30]. The mean difference scores between the two raters (MD inter) and between the two observations of the first rater (MD intra) were compared statistically using a one sample t-test. The within subsequent test differences was likewise tested in both groups using the paired t-test. MD inter is derived by calculating the mean of the differences between each pair of the two raters' observations. MD intra is derived by calculating the mean of the differences between each pair of the two observations of the first rater.

(a)

(b)

(c)

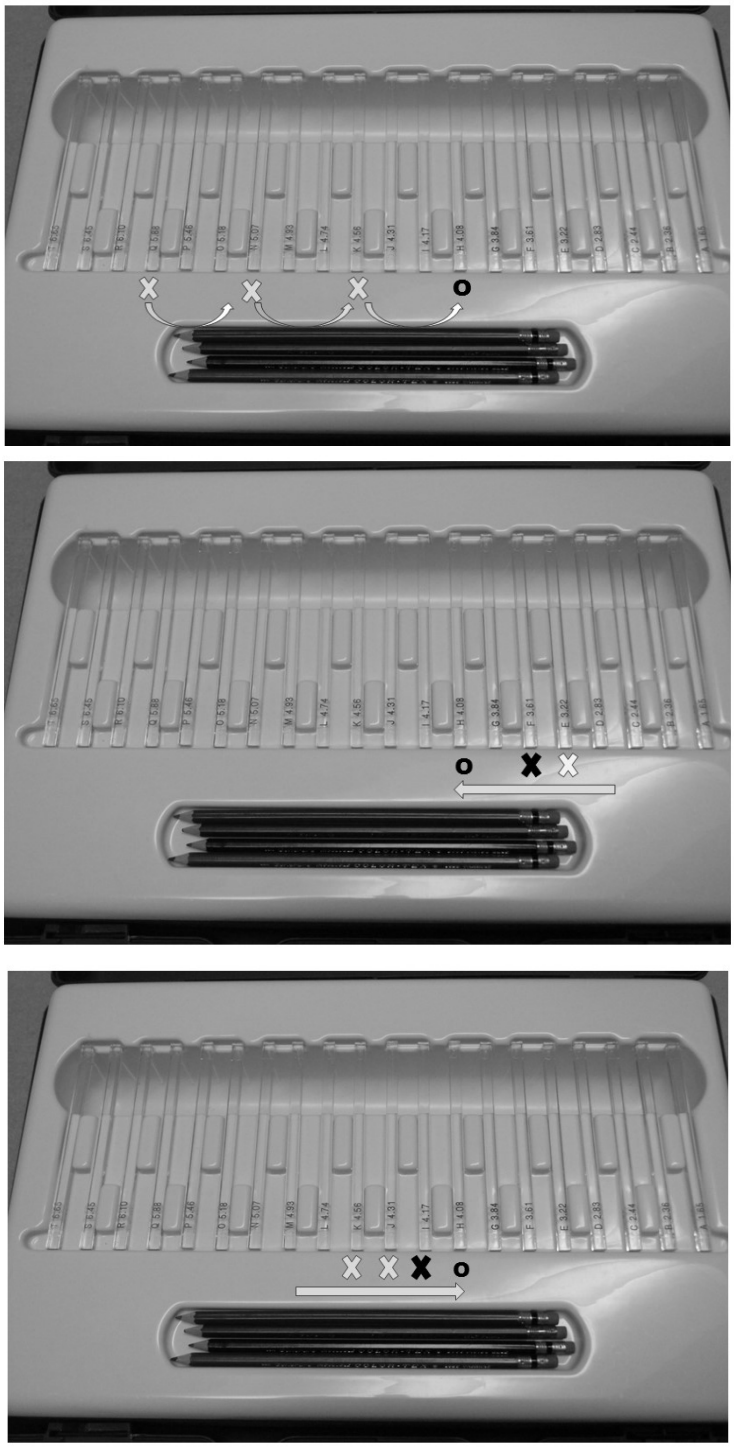

Figure 1-1 (a-c) Shows how the assessment of the TPT is performed

First step is the determination of the orientation series (orientation value: O) starting at the 5.88 monofilament, if felt by the participant subsequently the monofilament three steps lower was applied (repeating the next step every time three monofilaments lower) until no perception could be felt. The filament last felt constituted the orientation value. (b) The second step in the assessment of the TPT. The ascending series starting three steps below the orientation value (O) all filaments in this range are successively applied for 1.5 s until the first monofilament was felt X (this value is registered). (c) The descending series starting three steps above the orientation value (O) all filaments in this range are successively applied for 1.5 s until the subject reports its absence (the value of the last felt monofilament X is registered). These steps (Fig. 1b and 1c) were repeated three times resulting in an ‘‘ascending descending ascending descending ascending descending’’ (ADADAD) series.

1.3 RESULTS

1.3.1 Participants' characteristics

Participants were Caucasian, older than 18 and younger than 65, and in their aftercare phase of treatment (with mature scars). The control group (participants without scars) was age (4 years deviation maximum) and gender matched with the burn group. Eighteen burn patients and 18 age and gender matched healthy participants volunteered to take part in this study. In total, 36 people were tested by two raters. In each group more men (n = 13 or 72%) than women (n = 5 or 28%) were included and equal numbers of upper arms and lower arms were tested. The participants' characteristics of the burn group are illustrated in Table 1-1. In the burn group the major cause of the injury was thermal. Scar age was on average 83 months and average age of the participants was 43 years (range between 21 and 60 years, SD: 12.42 years). The age and gender paired-matched healthy participants were on average 43 years old (range between 21 and 63 years (SD: 12.18 years).

The mean TPT was significantly higher ($p < 0.001$) in the scar group (e.g., results from rater 1: 4.53 ± SD 0.75) than in the healthy controls (e.g., results from rater 1: 3.19 ± SD 0.67) as illustrated in Table 1-2. The mean values as well as the reliability are presented with dimensionless values as indicated on the monofilaments (not between values converted into grams).

Table 1-1 Participants' characteristics

Demographic variables scar group	
Sex % male-female	72-28
Average age in years (range, SD)	43 (21-60, 12.42)
Demographic variables control group	
Average age in years (range, SD)	43 (21-63, 12.18)
Location tested n (%)	
Upper arm volar	7 (39)
Upper arm dorsal	2 (11)
Lower arm volar	8 (44)
Lower arm dorsal	1 (6)
Cause of burn n (%)	
Thermal	14 (78)
Chemical	2 (11)
Electrical	2 (11)
Scar age	
Average age in months (range, SD)	83 (5-588,129.14)

n: number of participants; %: percentage, SD: standard deviation

1.3.2 Reliability of the ADADAD procedure performed with the SWM

1.3.2.1 Interrater reliability

As presented in Table 1-2 the interrater reliability was excellent in the scar group (ICC = 0.908/SEM = 0.212) and fair to good in the control group (ICC = 0.731/SEM = 0.121). As shown in Fig. 1-2 the TPT values of rater 1 and rater 2 are close to one another and were not significantly different in the burn scar group.

Table 1-2 Results of the interrater reliability analysis

	Rater 1.1 mean (SD)	Rater 2.1 mean (SD)	Inter ICC (95%CI)	MD inter (SD)	SEM	SEM%
scar	4.53 (.75)	4.58 (.65)	0.908 (.771-.964)	.05 (.30)	.212	4.67
healthy	3.19 (.67)	3.36 (.47)	0.731 (.414-.890)	.17 (.42)	.121	3.69
SD, standard deviation; ICC, intraclass correlation coefficient; MD, mean of differences; SEM, standard error of measurement difference; SEM%, standard error of measurement expressed in percentage of rater's mean						

1.3.2.2 Intrarater reliability

Results of the reliability analysis are summarised in Table 1-3. In the scar group intrarater ICC was excellent (ICC = 0.822/ SEM = 0.329). Within the control group also an excellent intrarater reliability (ICC = 0.807/SEM = 0.269) was found. As shown in Table 1-3 the intrarater reliability was lower in the healthy group (than in the burn group). In Fig. 1-2 the values of the different measurements are presented. In the control group (as shown in Fig. 1-2) the second measurement of the first rater was significantly higher ($p < .001$).

Table 1-3 Results of the intrarater reliability analysis

	Rater 1.1 mean (SD)	Rater 1.2 mean (SD)	Intra ICC (95%CI)	MD intra (SD)	SEM	SEM%
scar	4.53 (.75)	4.48 (.81)	0.882 (.585-.929)	.05 (.47)	.329	7.32
healthy	3.19 (.67)	3.57 (.58)	0.807 (.555-.923)	.38 (.39)	.269	7.95
SD, standard deviation; ICC, intraclass correlation coefficient; MD, mean of differences; SEM, standard error of measurement difference; SEM%, standard error of measurement expressed in percentage of rater's mean						

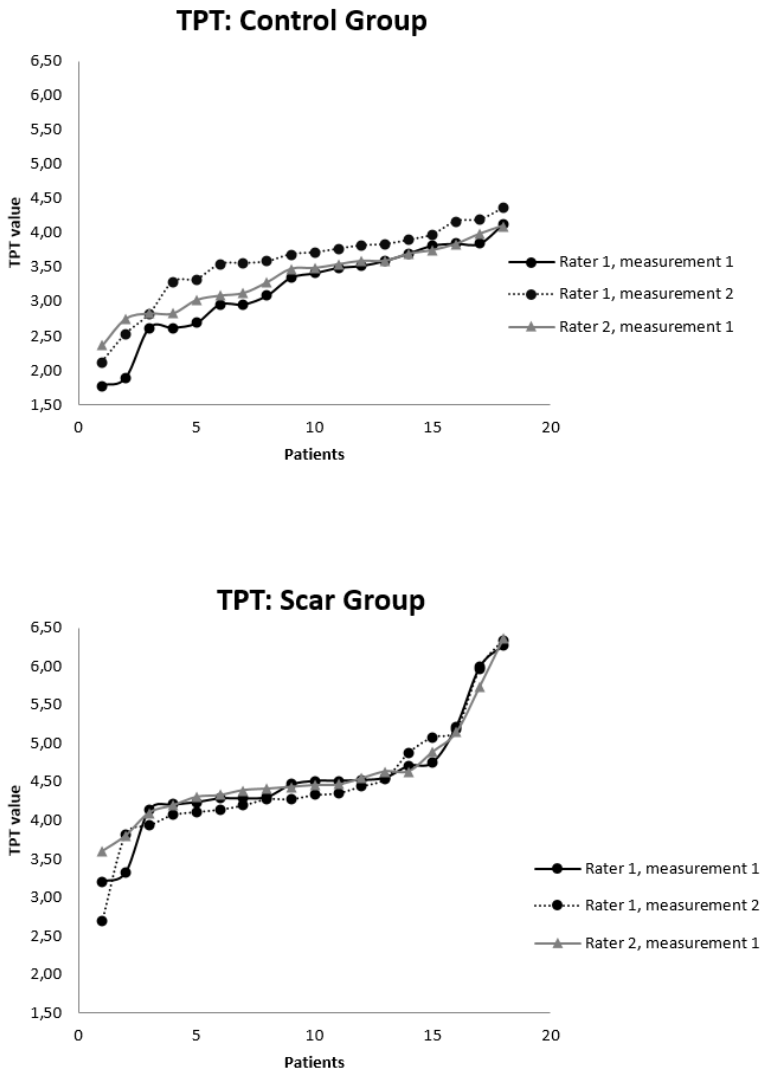

Figure 1-2 Scatter plot of the touch pressure (TPT) values in the control group and scar group

1.4 DISCUSSION

This study was set out with the aim of assessing the interrater and intrarater reliability of the 'ascending descending' procedure of the SWMT. It is to the best of our knowledge the first reliability study examining TPT within the burn population. Since sensation has been included as one of the core domains for burns outcome assessments[11], it under- lines the importance of evaluating hyposensibility after burn, thus assisting in the search for adequate treatments to improve tactile sensation in burn patients.

The current study found high ICC values for both interrater and intrarater reliability using the 'ascending descending' procedure in the scar group (ICC inter: 0.908/intra: 0.822) and control group (ICC inter 0.731/intra: 0.807). In addition the SEM and SEM% were calculated and

found to be low. In the scar group the SEM% were 4.67% and 7.32% for the interrater and intrarater reliability, respectively. In the healthy group the SEM% for interrater reliability was 3.69%, intrarater SEM% was 7.95%. For the interrater reliability the ICC values of the healthy group were significantly lower compared to the scar group. A possible explanation for lower reliability and higher variability in the retest values in the control group might be the smaller intervals between two consecutive monofilaments with smaller diameter (representing lower pressure in grams) in the lower part of the aesthesiometer. In the upper part of the aesthesiometer the pressure difference between two consecutive monofilaments is higher and probably more easily detectable[14]. The mean TPT was significantly higher ($p < 0.001$) in the scar group (4.53) than in the healthy controls (3.19), these results are consistent with those of other studies[6,31] and suggest that a lack of pressure perception might persist for several years after burn[3].

This procedure shows merit although a few reflections have to be made. Patients were recruited in a burn aftercare centre. The mean scar age was rather old, on average 83 months. Since a convenience population was used the reader is cautioned against generalising these findings to populations with less mature scars. In the selection of patients only upper extremity burn scars were included, because innervation density on the arms is different than on the soles of the feet. Generalisation of these findings to other body regions needs to be done with caution. The study of Tracey et al.[15] investigated overall young people, in contrast to this study where the age of the subjects ranged between 21 and 60 years old. Although it has been stipulated that there is limited influence of age in TPT[32], with ageing a reduction of Merkel and Meissner mechanoreceptors follows, and the number of myelinated peripheral nerve fibres diminishes[15,33]. A study investigating the variation of pressure perception in the index finger of various healthy age groups (between 19 and 88 years) revealed that threshold values were higher in elderly and more variation was noted with older age[33]. Further studies on the effect of age are therefore recommended. In spite of the rather high mean age and scar age, a strength of this study was the good match between the scar and the control group.

Due to pragmatic reasons the test and retest for the interrater reliability was performed on the same day, for the intrarater reliability the time varied between 9 and 12 days. Other authors examined test–retest reliability with an average of 7 days between measurements[15].

The ‘ascending descending’ procedure takes about 10 min and subjects need to stay focused and immobilised during the whole procedure. Environmental stimuli (e.g., noise, heat, light changes, etc.) were reduced to a minimum by testing in a quiet closed room with only the subject

(prone or supine position) and rater present, still these effects might have some influence on these findings.

Previous authors have described the 'ascending descending' procedure as too time-consuming for clinical practice[14], nevertheless it takes about 10 min to administer and with limited education on the procedure a rater can perform the test. In previous studies on TPT the measurement procedures in many cases differ from one another or the exact measurement procedure is not fully described. In contrast to earlier research a strength of this present study is the description of the 'ascending descending' test procedure. In the SWMT there is a slight gradation of pressure between two filaments and since the 'ascending descending' procedure is used in this study it seems less possible for the patients to know the order of presentation. These factors reduce the possibility of error and might explain the reliability of this procedure.

Further investigation could evaluate different test procedures (e.g., 'yes–no', 'forced choice', etc.) in order to determine the most reliable and feasible procedure. Ameliorating tactile sensation is often a goal during scar aftercare treatment. Since the TPT measurement is being used (e.g., in Oscare) in the aftercare settings to evaluate sensibility changes over time and evaluate the effect of treatment, in future research the responsiveness of the SWMT should be investigated in the burn population. Each one of the 20 filaments are labelled so as to give a linear scale of perceived intensity which exerts a specific, repeatable force between 0.86 g and 448 g. These forces were converted into a logarithmic function by the manufacturers (labelled units on the monofilaments = Log^{10} (10 x force in milligramme)). For further research a good recommendation would be to use a force transducer to measure the exact force of each monofilament. Weinstein et al.[32] described that the values in grams are not reliable to use in statistical analysis. Establishing a relation between hyposensibility and functional status (e.g., hand function) and quality of life in patients with burn scars would be interesting to affirm whether these deficits influence human functioning. Future studies should focus more on evaluating the effect of therapeutic interventions on skin sensation (and pain and pruritus) taking into account patient factors (e.g., age, scar age), injury factors (e.g., cause of burn, burn depth, surgical intervention). Recent studies have investigated the above mentioned effects with vacuum massage[34], manual scar massage[35] and found promising results.

In conclusion this study shows that the SW aesthesiometer with the 'ascending descending' measurement procedure is a feasible and reliable objective measure to evaluate TPT in (older burn) upper extremities scars as well as in healthy subjects. Further research with a larger sample size, various body location and different scar ages is needed to support present findings.

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2 THE SCARBASE DUO ® INTRARATER AND INTERRATER RELIABILITY AND VALIDITY OF A COMPACT DUAL SCAR ASSESSMENT TOOL

Published as:

Fell M, Meirte J, Anthonissen M, Maertens K, Pleat J Moortgat P The Scarbase Duo®: Intrarater and interrater reliability and validity of a compact dual scar assessment tool. Burns 2016;42(2):336-44 doi: 10.1016/j.burns.2015.08.005.

Abstract

Objective scar assessment tools were designed to help identify problematic scars and direct clinical management. Their use has been restricted by their measurement of a single scar property and the bulky size of equipment. The Scarbase Duo® was designed to assess both trans-epidermal water loss (TEWL) and colour of a burn scar whilst being compact and easy to use.

Twenty patients with a burn scar were recruited and measurements taken using the Scarbase Duo® by two observers. The Scarbase Duo® measures TEWL via an open-chamber system and undertakes colorimetry via narrow-band spectrophotometry, producing values for relative erythema and melanin pigmentation. Validity was assessed by comparing the Scarbase Duo® against the Dermalab® and the Minolta Chromameter® respectively for TEWL and colorimetry measurements.

The intra-class correlation coefficient (ICC) was used to assess reliability with standard error of measurement (SEM) used to assess reproducibility of measurements. The Pearson correlation coefficient (r) was used to assess the convergent validity.

The Scarbase Duo® TEWL mode had excellent reliability when used on scars for both intra- (ICC= 0.95) and interrater (ICC= 0.96) measurements with moderate SEM values. The erythema component of the colorimetry mode showed good reliability for use on scars for both intra- (ICC= 0.81) and inter-rater (ICC= 0.83) measurements with low SEM values. Pigmentation values showed excellent reliability on scar tissue for both intra- (ICC= 0.97) and interrater (ICC = 0.97) with moderate SEM values. The Scarbase Duo® TEWL function had excellent correlation with the Dermalab® (r= 0.93) whilst the colorimetry erythema value had moderate correlation with the Minolta Chromameter® (r= 0.72).

The Scarbase Duo® is a reliable and objective scar assessment tool, which is specifically designed for burn scars. However, for clinical use, standardised measurement conditions are recommended.

2.1 BACKGROUND

Survival after severe burns and trauma has dramatically improved over the last decade but this has not always been paralleled with a similar increase in quality of life. Patients have to contend with the sequelae of scarring, which can lead to an array of appearance-related, psychological and functional problems. Scars represent a significant challenge to the multidisciplinary care team and a large burden on the resources of health care systems. Research into the area of improving treatment options for scarring is relevant both on an individual and a societal level[1].

Scar assessment tools are used for monitoring the quality of scars against time, the effect of treatments and for comparing scars. The ideal scar assessment tool needs to be reliable (error of measurement), valid (measures what it is meant to measure) and feasible (easy to administer with minimal patient burden). Scar assessment can be achieved via subjective or objective methods. Subjectively, scars can be assessed by patients, clinicians/medical professionals and third party observers. However, subjective scales can be unreliable due to a great variability in interpretation[2]. Various assessment scales have been created but the most commonly used are the Vancouver Scar Scale (VSS) and the Patient Observer Scar Assessment Scale (POSAS)[3–5]. Objective scar assessment has an advantage over subjective assessment because the reliability of measurements between observers tends to be greater[6].

Objective scar assessment tools can provide a quantitative measurement of physiological or physical scar parameters. Physiological properties include trans-epidermal water loss (TEWL), hydration, perfusion and trans-cutaneous oxygen level. Physical properties include colour, elasticity, topography and planimetry[6].

TEWL is an important physiological marker to measure the efficiency of the human skin barrier to retain water[7]. The hydration and water content of skin is important as it helps to maintain normal skin turgor and texture and is strongly related to TEWL. TEWL can be used as an indirect measurement of the barrier function of skin because when skin is damaged, as is the case during scarring, TEWL increases[8]. Open chamber devices are the most common method of measuring TEWL. They detect the water vapour gradient near the surface of the skin based on the principle of Fick's law of diffusion[9].

Scar colour is a key physical property because its comparison to uninjured, surrounding skin is correlated with relative patient satisfaction and reflects biological processes within the scar[10]. Colour assessment forms a component of subjective scar assessment scales because patients commonly are dissatisfied with a mismatch of scar colour compared to their surrounding skin. Clinically, colour assessment is useful as an indicator of the scar maturation and as an early,

quantifiable index of the likelihood of the scar becoming hypertrophic[11,12]. The colour of a scar is a complex physical property that is contributed to by three main components (brown melanin pigment, red oxyhemoglobin and yellow bile). Colorimetry tools commonly assess the colour of scars via tristimulus reflectance colorimetry (the level of light reflected from the scar surface) or narrow-band spectrophotometry (the absorption of light in the scar)[6].

Objective scar assessment tools have predominantly tested a single characteristic of the scar and their use has largely been restricted to the research settings due to their bulky, impractical size. Anthonissen et al. were the first authors to report about the utility of a dual scar assessment device called the Dermalab® (Cortex Technology, Hadsund, Denmark); this measures both elasticity and TEWL via a single central unit[7]. A new device called the Scarbase Duo® (Courage Khazaka, Cologne, Germany), calculating TEWL and colorimetry, has been designed to be small, easy to use and affordable. The aim of this study was to assess intra- and interrater reliability, validity and feasibility of the Scarbase Duo® for use in research and clinical application.

2.2 METHODS

This study was designed in accordance with the Guidelines for reporting reliability and agreement studies[13].

2.2.1 Patients and observers

Patients were recruited from the OSCARE Centre (Burns and Scar Aftercare Centre) in Antwerp, Belgium over a three week testing period. Patients were eligible when they were at least 16 years old with scars in the active phase of healing after complete wound closure. Previous treatment for these scars followed a clinical protocol and was recorded in each patient. Patients who were unable to provide consent due to a language barrier or psychiatric disorder were excluded. Scars had to be situated on the upper or lower limbs with the exclusion of the hands, feet, trunk or head and neck. These chosen sites have been shown to have lower and more consistent rates of TEWL[14]. Contralateral areas of healthy skin were used for comparison and in cases where these too were scarred, adjacent healthy skin was tested. The two observers collecting the data were a clinician and physiotherapist. The study protocol was approved by the ethics committee of the Hospital Network Antwerp (ZNA), Belgium (Ethical committee 009OG031, study number EC4549).

2.2.2 The Scarbase Duo

The Scarbase Duo® (Courage + Khazaka, Cologne, Germany) device consists of a main unit, two probes and a sensor for room temperature and humidity. The probes, one for the Tewameter® (TEWL) and one for the Mexameter® (colorimetry), attach to the main unit via independent leads into separate channel inputs (see Fig. 2-1).

Figure 2-1 The Scarbase Duo ®

The Scarbase Duo ® when linked up to a laptop. There are 4 components displayed: the central unit, the temperature sensor, the Tewameter probe and the Mexameter probe.

2.2.2.1 TEWL mode

The Tewameter® (see Fig. 2-2) open chamber probe consists of a hollow tube (1 cm x 2 cm) containing combined humidity and temperature sensors, positioned at different heights above the skin surface. The local relative humidity and temperature are recorded at both sites and a corresponding vapour pressure is calculated automatically. TEWL is expressed in grams per square metre per hour ($g/m^2/h$). At the start of each testing day, the Tewameter® was calibrated. In order to measure TEWL correctly, the open chamber was held perpendicular to the scar or skin surface and away from a direct light source. The small size of the chamber minimised the local airflows known to distort open chamber results[15]. Patients were asked to turn their face away from the Tewameter®

when testing so that the air currents of breathing did not interfere with assessments. Measurements were stopped after 30 s (time required for TEWL equilibrium to be reached[16]) and the mean/standard deviation of the TEWL measurements were recorded.

Figure 2-2 The Tewameter® probe to measure trans-epidermal water loss

2.2.2.2 Colorimetry mode

The Mexameter® (see Fig. 2-3) utilises narrow-band spectrophotometry to measure the vascularity and pigmentation (called erythema and melanin respectively) of the skin based on differences in absorption of red and green light. The haemoglobin component of skin reflects red light and absorbs green whilst the brown of the melanin component absorbs light of all wavelengths. The distal end of the probe is equipped with a spring mechanism which calculates the colour characteristics when a defined pressure is reached on the skin surface. A separate measurement was created for erythema and melanin. Measurements range from 1 to 1000 for both the erythema and melanin index with higher readings representing more erythematous and darker pigmentation respectively. Three measurements were taken in succession and mean values were calculated.

Figure 2-3 The Mexameter® probe to measure colorimetry

2.2.3 Instruments to test for validity

2.2.3.1 Dermalab®

TEWL was assessed by the Dermalab® (Cortex Technology, Hadsund, Denmark) which is an open chamber system, similar in design to the Tewameter®. The TEWL component of the Dermalab® is regarded as a typical open chamber TEWL device and has been used experimentally before as a baseline for validity due to its accurate and concise measuring mechanism [16,17]. The Dermalab® has not previously been validated for testing TEWL in scars [7].

2.2.3.2 The Chromameter®

The Minolta Chromameter® (Minolta Camera Co., Osaka, Japan) utilises tri-stimulus reflectance colorimetry according to the Commission International de L'Eclairage system producing a three dimensional measurement (L* represents the relative brightness (with a scale of 0–100), a* represents the range of green (-60) to red (60) reflected light, and b* represents the range of blue (-60) to yellow (60) reflected light). Higher values for a* correspond with increasing redness of the scar[18]. The Chromameter® has shown excellent intra- and interrater reliability along with moderate correlation to the colour and vascularity component of the POSAS scale [19]. Three separate measurements were taken by the Chromameter® and mean values for the L*, a* and b* were calculated.

2.2.4 Measurement procedure

Informed written consent was obtained from all patients. Thirty minutes before measurements were taken, patients acclimatised to the testing environment by waiting in the testing room, in the position in which they were to be tested and with the scars and corresponding healthy skin uncovered. The patients were in a sitting position for scars on the upper limb and a lying position

for scars on the lower limb. Testing was performed in the same room with room temperature and humidity recorded immediately prior to the start of measurements being taken. Care was taken to place the temperature and humidity sensor away from any heat source (e.g. patient or computer). The boundaries of the test sites were marked with circular adhesive markers.

Two consecutive measurements were taken by the first rater for TEWL and colorimetry using the Scarbase Duo® on the scar and healthy skin. The first rater then measured the same areas with the Chromameter® and the Dermalab®. The second rater conducted a single measurement for TEWL and colorimetry using the Scarbase Duo® on the identical scar and healthy skin sites. A period of four minutes was observed between any TEWL measurement or any colorimetry measurement. This allowed both equilibrium time for condensation in the TEWL probe (=zero-drift) and the skin capillary refill time recovery after pressure from the colorimetry device[7].

2.2.5 Statistical analysis

Statistical analysis was performed using the statistical programme SPSS v20.0 (Armonk, NY: IBM Corp.).

2.2.5.1 Reliability

Reliability refers to the consistency of the assessment tool measurements (i.e. whether measurement is the same when no real change has occurred). The intra-class correlation coefficient (ICC) with its 95% confidence interval was used to measure the intra- and interrater reliability on scars and normal skin[20]. A two-way random-effect model and absolute agreement was selected and calculated for all of the scores. The Fleiss and Shrout classification for reliability coefficients (ICC2,1) was used to describe the degree of reliability[20]. The single measure ICC was used to interpret the results. Reliability was judged to be good if the ICC was >0.75, moderate 0.4–0.75 or poor <0.4[21]. The reproducibility of the Scarbase measurements was deduced via the standard error of measurement (SEM), calculated by dividing the standard deviation of the difference between mean scores at baseline and follow-up (SDd) by the square root of two (SEM = SDd/√2). This quantifies the variability of the difference scores and is referred to as the typical error of differences[22]. Bland–Altman plots and limits of agreement were used to analyse the repeatability of a single measurement method and to compare measurements between two raters[23].

2.2.5.2 Validity

Validity refers to the truth of the assessment tool measurements (i.e. whether the tool is measuring what it is meant to). Tests of validity are indirect and rely on comparison against a method believed to be correct. Pearson's correlation coefficients were calculated to assess the convergent validity of the Scarbase Duo® compared to other assessment tools. Validity was judged to be good if the Pearson's correlation or the ICC was >0.6, moderate 0.3–0.6 or poor <0.3[21]. Where necessary,

data was transformed using linear regression scales. Bland–Altman plots and limits of agreement were used to analyse the agreement of the two measurement methods[23].

2.3 RESULTS

2.3.1 Patient and scar characteristics

Twenty burn scars were included from 20 Caucasian patients, 16 of whom were male with a mean age of 45 years (SD=18.22). Eleven of the scars were located on the arm (4 upper arm and 7 forearm) and 9 were located on the leg (5 upper and 4 lower leg) with an overall mean scar age of 5.65 months (SD=5.76). Eight of the scars had healed spontaneously with the remaining twelve having received a split skin graft. Taking into account the definition of hypertrophic scars[24] and the correlation between scar redness and scar thickness[11], we identified that eighteen out of the twenty scars had developed into hypertrophic scars.

The values for Tewameter® TEWL in healthy skin and scars ranged from 3.7 to 12.4 g/m^2/h (mean= 6.3, SD= 2.5) and 4.9 to 26.0 g/m^2/h (mean=9.9, SD= 5.2) respectively. The values for the Mexameter® erythema in healthy skin and scars ranged from 115.7 to 343.3 (mean= 215.0, SD= 66.3) and 297 to 648 (mean= 449.6, SD= 86.76) respectively. The values for the Mexameter® pigmentation in healthy skin and scars ranged from 56.3 to 317.67 (mean= 162.1, SD= 76.6) and 6.7 to 374.0 (mean= 161.7, SD= 85.2) respectively.

2.3.2 Reliability

2.3.2.1 Tewameter®TEWL values

The ICC values ranged from 0.87 to 0.95 for the intra-rater and 0.9 to 0.96 for interrater reproducibility. This showed good to excellent correlation for repeated TEWL measurements and was combined with moderate SEM values (see Table 2-1). The Bland–Altman plots for the intra- and inter-rater agreement of two measurements on scars show that the bias of the mean is low, suggesting that no systematic error could be detected. The limits of agreement are far apart, suggesting that the high correlation between the repeated measures and the two raters is not supported by a high agreement (see Fig. 2-4).

Tabel 2-1 ICCs and SEMs for the intra- and inter-rater reliability of the trans-epidermal water loss measurements with the Tewameter®. Measurements were taken on scars and adjacent healthy skin. A 95% confidence interval is marked between brackets

	Type	Mean[a]	SD[a]	ICC (95%CI)	SEM
Intrarater reliability	Scar	9.83	5.32	0.95 (0.89-0.98)	1.17
	Healthy skin	6.05	2.3	0.87 (0.66-0.95)	0.74
Interrater reliability	Scar	9.97	5.53	0.96 (0.9-0.98)	1.12
	Healthy skin	6.23	2.21	0.9 (0.78-0.96)	0.75
[a] Values expressed in g/m^2/h.					

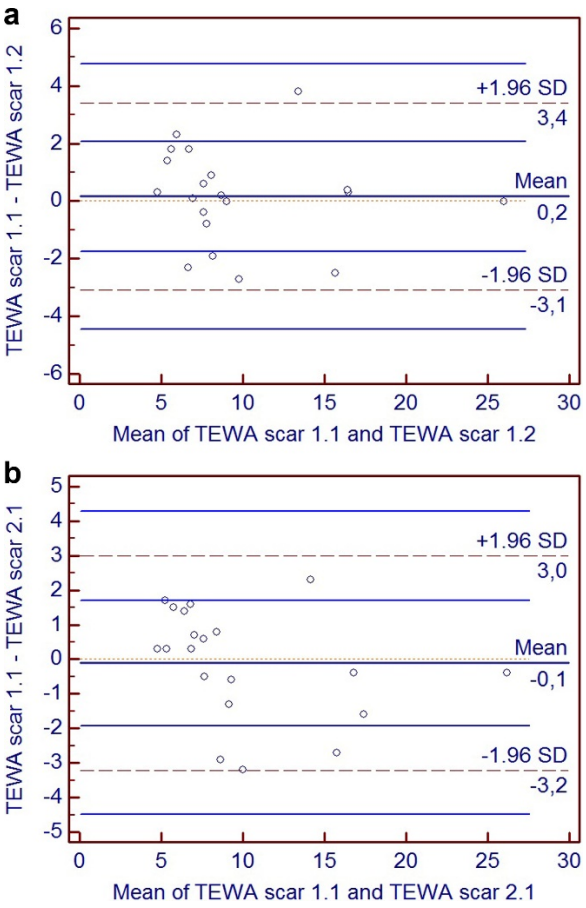

Figure 2-4 Bland-Altman plots for the Tewameter intra (1.1-1.2) and inter (1.1-2.1) rater agreement on scars (plates a and b).

2.3.2.2 Mexameter® erythema values

The ICC values ranged from 0.81 to 0.94 for the intra-rater and 0.83 to 0.96 for the interrater reproducibility. This showed good to excellent correlation for repeated erythema measurements, which was combined with relatively low SEM values (see Table 2-2). The Bland–Altman plots of the intra- and interrater agreement of two measurements in scars show the bias of mean to be low, suggesting that no systematic error could be detected. The limits of agreement are far apart, but this could be due to a few outliers. 85% of the mean differences are within the acceptable limits of agreement (see Fig. 2-5).

Table 2-2 ICCs and SEMs for the intra- and inter-rater reliability of the erythema measurements with the Mexamater ®. Measurements were taken on scars and adjacent healthy skin. A 95% confidence interval is marked between brackets.

	Type	Mean[a]	SD[a]	ICC (95%CI)	SEM
Intrarater reliability	Scar	453	8.92	0.81 (0.58-0.92)	39.75
	Healthy skin	210.54	68.03	0.94 (0.84-0.98)	15.74
Interrater reliability	Scar	452.2	452.2	0.83 (0.63-0.93)	38.88
	Healthy skin	215.24	67.5	0.96 (0.91-0.99)	13.36

[a] Values expressed in arbitrary units.

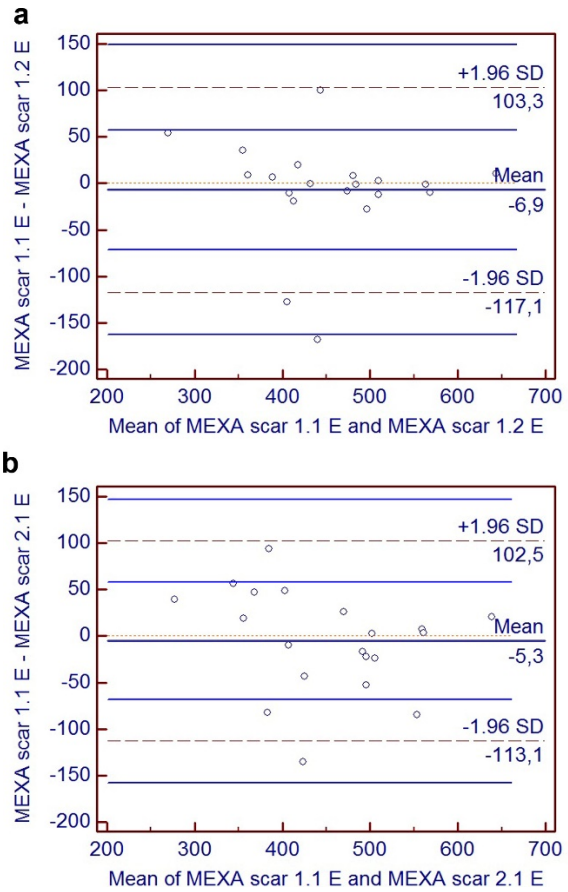

Figure 2-5 Bland-Altman plots for Mexameter erythema intra (1.1-1.2) and inter (1.1-2.1) rater agreement on scars (plates a and b).

2.3.2.3 Mexameter® pigmentation values

The ICC values ranged from 0.96 to 0.97 for intra-rater and 0.97 to 0.99 for intrarater reproducibility. This showed excellent correlation for repeated pigmentation measurements and was combined with moderate SEM values on scarred skins and relatively low SEM values on healthy skin (see Table 2-3). The Bland–Altman plots for the intra- and interrater agreement of two measurements on scars show the bias of the mean to be low, suggesting that no systematic error could be detected. The limits of agreement are far apart, suggesting that the high correlation between the repeated measures and the two raters is not supported by a high agreement (see Fig. 2-6).

Table 2-3 ICCs and SEMs for the intra- and inter-rater reliability of the pigmentation measurements with the Mexamater®. Measurements were taken on scars and adjacent healthy skin. A 95% confidence interval is marked between brackets.

	Type	Meana	SDa	ICC (95%CI)	SEM
Intra-rater reliability	Scar	115.69	85.44	0.97 (0.92-0.99)	15.52
	Healthy skin	162.51	77.65	0.97 (0.93-0.99)	13.35
Inter-rater reliability	Scar	114.27	80.42	0.97 (0.92-0.99)	14.58
	Healthy skin	161.81	76.84	0.99 (0.97-0.99)	8.71
[a] Values expressed in arbitrary units.					

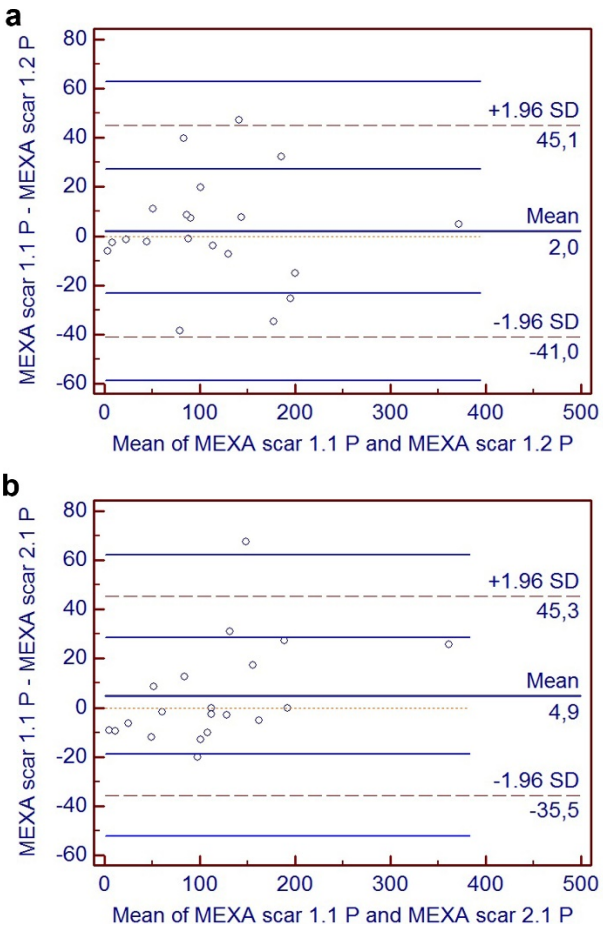

Figure 2-6 Bland-Altman plot for the Mexameter pigmentation intra (1.1-1.2) and inter (1.1-2.1) rater agreement on scars (plates a and b)

2.3.3 Validity

2.3.3.1 Validating TEWL values from the Tewameter® function of the Scarbase Duo® against the Dermalab®

The ICC value and the Pearson correlation coefficient (ICC= 0.81, r= 0.93) show good to excellent correlation for scars between the Tewameter® and the Dermalab®. Moderate correlation (ICC= 0.52, r= 0.72) is shown between the two tools on healthy skin (see Table 2-4). The Bland–Altman plots for agreement between the two tools on scars show us that the bias of the mean is high, suggesting that a systematic error could be detected. The Dermalab® TEWL probe systematically measures approximately 2.5 g/m^2 higher than the Tewameter® TEWL probe. The limits

of agreement are far apart, suggesting that the high correlation between the two measurement methods is not supported by high agreement (see Fig. 2-7).

Table 2-4 Concurrent validity of the TEWL measurements on scarred and healthy skin between the Tewameter of the Scarbase Duo ® and the Dermalab ®.

Type	Mean Scarbase Duo [a]	Mean Dermalab [a]	ICC (95%CI)	Pearson r
Scar	9.91	12.75	0.81 (0.23-0.94)	0.93
Healthy	6.34	8.74	0.52 (0.02-0.79)	0.72
[a] Values expressed in g/m^2/h				

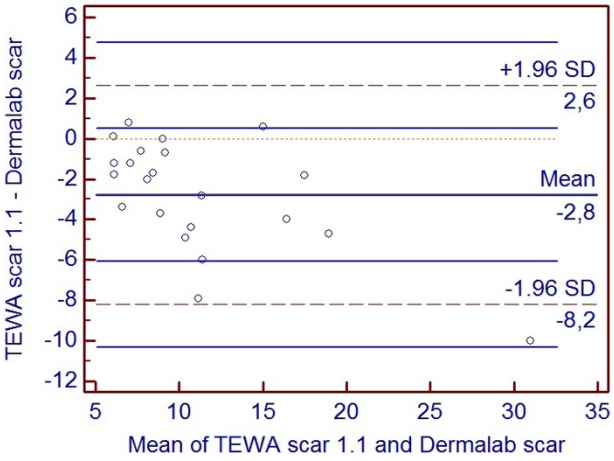

Figure 2-7 Bland-Altman plots for the agreement of transepidermal loss assessment between the Tewameter and the Dermalab on scar.

2.3.3.2 Validating erythema values from the Mexameter® function of the Scarbase Duo® against the Chromameter® a values*

The ICC values and the Pearson correlation coefficient (ICC=0.47, r= 0.72) show moderate to good correlation for scars between the Mexameter® erythema values and the Chromameter® a* values. Excellent correlation (ICC= 0.93, r= 0.93) is seen between the two measurement methods on healthy skin (see Table 2-5). The Bland–Altman plots for the intra- and inter-rater agreement of two measurements on scars show us that the bias of the mean is low, suggesting that no systematic error could be detected. The limits of agreement are far apart, suggesting that the high correlation between the two measurement methods is not supported by a high agreement (see Fig. 2-8).

Table 2-5 Concurrent validity of colorimetry measurements on scarred and healthy skin between the Mexameter® erythema values of the Scarbase Duo® and the Minolta Chromameter® a- values.*

Type	Mean Scarbase Duo [a]	Mean Chromameter [a] (transformed)	ICC (95%CI)	Pearson r
Scar	449.45	215	0.47 (-0.11-0.8)	0.72
Healthy	447.17	216.65	0.93 (0.83-0.97)	0.93
[a] Values expressed in arbitrary units				

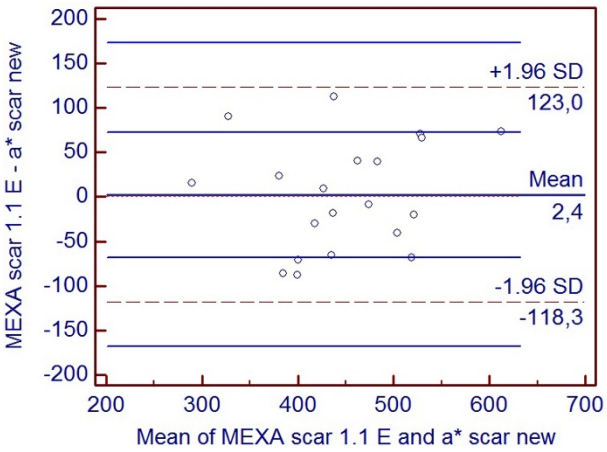

Figure 2-8 Bland-Altman plots for the agreement between the Mexameter erythema values and the Chromameter a values on scar.*

2.4 DISCUSSION

The Scarbase Duo® has been designed to assess two objective qualities within the scar (TEWL via the Tewameter® and colorimetry via the Mexameter®), to be compact and easy to use. The Scarbase Duo® was shown to be reliable with good to excellent correlation for repeated measurements and between two observers (ICC ≥ 0.81) with low to moderate SEM values. These results correspond with an earlier study concerning the inter-rater reliability of the Mexameter® on scars, although intrarater reliability has not previously been investigated[24]. The Tewameter® has been shown to be able to differentiate normal skin from mildly disrupted skin surface but has never before been tested on scars[25]. The results found in this report for the Tewameter® are slightly favourable to the findings of Anthonissen and co-workers for the Dermalab®[7].

Bland–Altman plots and the limits of agreement only show high agreement for the Mexameter® erythema values. This is not surprising since objective assessment of scar colour and trans-epidermal loss are dependent upon several endogenous, exogenous and environmental factors[26]. The discrepancy between the high correlation values and the moderate agreement can be related to the heterogeneity of the study population and could be investigated on a more homogenous population in the future.

The ICC values and the Pearson correlation coefficient showed good to excellent correlation for scars between the Tewameter® and the Dermalab®. Moderate correlation was found for measurements taken on healthy skin. The Bland– Altman plots for the intra- and interrater agreement of two measurements on scars show that the bias of the mean is high, suggesting that a

systematic error could be detected. The Dermalab® TEWL probe systematically measured 2.5 g/m^2/h higher than the Scarbase Duo® TEWL probe. A linear regression analysis established a statistically significant correlation between both measurement methods. The regression equation was: Tewameter® value= 0.76xDermalab® value.

The difference between the two could be due to different calibration methods. One should also take into account that the absolute value of one TEWL measurement ranges between 5 and 20 mg. To convert this value into g/m^2/h increases the risk of systematic error. Therefore, we suggest to use arbitrary units to report TEWL in the future.

The ICC values and the Pearson correlation coefficient showed moderate to good correlation for scars between the Mexameter® erythema values and the Chromameter® a* values. In healthy skin the two tools had excellent correlation. The Bland–Altman plots for the intra- and interrater agreement of two measurements on scars show us that the bias of the mean is low, suggesting that no systematic error could be detected. The limits of agreement are far apart, suggesting that the high correlation between the two measurements is not supported by a high agreement. A linear regression analysis established a statistically significant correlation between both measurement methods. The regression equation was: Mexameter® erythema value= 27.02xChromameter® a* value.

The most influencing factors for this moderate correlation between the two measurement methods are likely to be the differences in maintaining even pressure to avoid blanching of the scar and the difference in skin measuring area, which permits the influence of differing scar texture. The two devices also make use of different colour assessment methods as the Mexameter® is a narrow band spectrophotometry device whereas the Chromameter® utilises a tri-stimulus reflectance colorimeter. This makes comparison between the two tools even more difficult. We comment on the feasibility of the Scarbase Duo through our experience of using the tool during the testing process. The Scarbase Duo® consists of a small, light body with two small probes and immediate data logging on to the computer. A computer is always needed, which makes bedside testing difficult, but adds to uniform data storage and the software is easy to use. The Tewameter® probe is an open-chamber system, and in our experience we recommend the use of an air shield to avoid turbulence at the measurement site. The possibility of on-site calibration of the Tewameter® probe is advantageous. More details regarding the accurate usage of an open-chamber TEWL device can be found in previous literature[9]. Design advantages of the Mexameter® probe include the spring-mounted central portion which maintains even pressure per measurement[24], whereas the Chromameter® can cause blanching of the skin when too much pressure is applied. The meaning of

the Mexameter® erythema value is more comprehensible than the meaning of the Chromameter® a* value.

2.5 CONCLUSION

The Scarbase Duo® is a reliable and valid objective scar assessment tool which has been specifically designed for use in burn scars. Scar erythema and trans-epidermal water loss are two valuable predictors of burn scar maturation, and as such the Scarbase Duo® can help to evaluate the effects of different treatment protocols and develop practice guidelines for burn scar management. For the detection of individual clinical differences, we believe that this device may be suitable, but further investigation on a more homogenous population seems appropriate and standardised measurement conditions are recommended.

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3 CLASSIFICATION OF QUALITY OF LIFE SUBSCALES WITHIN THE ICF FRAMEWORK IN BURN RESEARCH: IDENTIFYING OVERLAPS AND GAPS

Published as:

Meirte J, van Loey NEE, Maertens K, Moortgat P, Hubens G, Van Daele U. Classification of quality of life subscales within the ICF framework in burn research: Identifying overlaps and gaps. Burns 2014:1–7. doi:10.1016/j.burns.2014.01.015

Abstract

Quality of life (QOL) is one of the leading outcomes in burn care research. This study classifies subscales of common QOL measures within the International Classification of Functioning disability and health (ICF) framework to determine to which extent the measures are complementary or overlapping and to investigate whether the instruments are able to describe the full spectrum of patients' functioning.

A literature search was performed to determine the most frequently used questionnaires in burn research. The subscales of the three mostly used questionnaires were classified within the ICF framework.

Two generic measures, the Short Form-36 items (SF-36) and the European Quality of Life 5 Dimensions (EQ-5D), and a disease specific measure, the Burn Specific Health Scale-Brief (BSHS-B), were analysed. The BSHS-B covered most domains and was the only scale that included personal factors. The SF-36 included only one domain in the activity limitations and similar to the EQ-5D no contextual factors were included. Environmental factors were not addressed in the questionnaires, even though these may have an impact on the quality of life in patients with burns.

To capture the full spectrum of dysfunctioning a combination of the BSHS-B with a generic questionnaire seems obligatory. However still some domains of functioning remain uncovered.

3.1 INTRODUCTION

Two decades ago, the World Health Organisation (WHO) defined quality of life (QOL) as ‘‘an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person’s physical health, psychological state, personal beliefs, social relation- ships and their relationship to salient features of their environment’’[1,2]. Since then, QOL has received increasing attention, including in burn populations, and a burgeoning body of research documented burn survivors’ health-related quality of life (HRQOL)[3–7].

In burn research various generic HRQOL self-report measures have been used. The most common burn specific questionnaire available is the Burn Specific Health Scale (BSHS) that has a long history of several adaptations[4,8,9]. The most frequently used version in recent years is the Burn Specific Health Scale Brief (BSHS-B) that has been translated in several languages all over the world[4,10]. The BSHS-B has been shown to be measurement invariant across two European countries, indicating its stability across cultures[11]. However, it is currently unclear to which extent the BSHS- B and generic HRQOL measures are complementary or overlapping in measuring different aspects of HRQOL following burns and whether the full spectrum of disability is captured by using (a combination of the) questionnaires.

To elucidate which HRQOL aspects are covered by the currently used self-report measures a broad bio-psycho- social framework is of interest. The International Classification of Functioning Disability and Health (ICF) is a worldwide used framework to describe the health condition of a patient in such a context. The ICF inventories all domains of disability from body, individual and societal perspectives[12]. As presented in Fig. 3-1, disability involves dysfunctioning at one or more of these levels: impairments in body function or structures, activity limitations and participation restrictions. The environmental factors (physical and social environment) and the personal factors, such as age, gender and marital status, may influence human functioning in a positive or negative manner. In sum, the ICF enables the understanding of phenomena related to function that may be particularly relevant when assessing quality of life following burns.

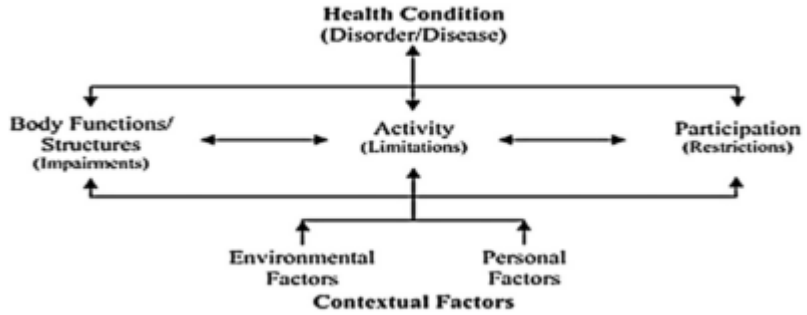

Figure 3-1 Illustration of the international classification of functioning, disability and health by the World Health Organisation

Despite the growing attention for functional outcome during the last fifteen years in burn research the limited application of HRQOL measures within the ICF framework is notable with very few burn articles on this subject[12,13]. One review on functional outcome identified seven core domains that were considered essential to comprehensively assess outcome after burns[15]. The core domains proposed are skin, neuromuscular function, sensory and pain, psychological function, physical role function, community participation and perceived quality of life, but it is unclear to which extent the proposed domains are captured in the most commonly used self-report measures. In a systematic review concepts of common outcome measures in burn care were considered within the ICF framework using standardised linking rules. HRQOL questionnaires were included in this study and it was reported that 43 concepts (out of 50) of the BSHS-B could be linked to the ICF[14]. In clinical practice, however, the interpretation of the outcome is often based on the subscale scores of the questionnaires, rather than interpreting the distinct items. Currently, no reports are available linking the subscales of the HRQOL questionnaires to the ICF framework in an attempt to describe functioning following burns.

The aim of this study is to classify the subscales of frequently used HRQOL measures within the ICF and to answer the question if these instruments are able to describe the broad spectrum of patients' functioning. Moreover this paper seeks to address the following questions: What aspects of HRQOL do the different questionnaires measure? What aspects of HRQOL are left uncovered? Which different domains of ICF are covered by each questionnaire?

3.2 METHODS

3.2.1 Selection procedure

The electronic database PubMed was searched for English- language empirical studies, published between 1990 and 2013 using a combination of Medical Subject Headings (Mesh).The Mesh terms 'Quality of life' and 'Burns' were combined with the following three keywords: 'Questionnaires', 'Outcome Assessment (Health Care)' and 'Survey'. Articles on children, burns other than skin burns (e.g., eye burns, inhalation injury) and other outcome measures were excluded. After screening the abstracts and the full texts this search yielded 30 articles in which seven HRQOL questionnaire were used: the European Quality of Life 5 Dimensions (EQ-5D), the Short Form-36 Medical Outcomes Survey (SF-36), the Sickness Impact Profile (SIP), the Quality of Life Questionnaire (QLQ), the Quality Of Life Scale (QOLS), the Burn Specific Health Scale (with all its variants) and the Dermatology Life Quality Index (DLQI) (Fig.3-2). We selected the three most commonly used questionnaires. As shown in Fig. 3-2, within the burn population the BSHS-B[5,7,9,10,16–25], the SF-36[16,18,20–23,26–32] and the EQ-5D[3,16,33–35] appear the most frequently used HRQOL measures in recent literature in contrast to the SIP[36], the QLQ[26,27], the QOLS[37] and the DLQI[38]. Subsequently the BSHS-B, the SF-36 and the EQ-5D were retained for further investigation.

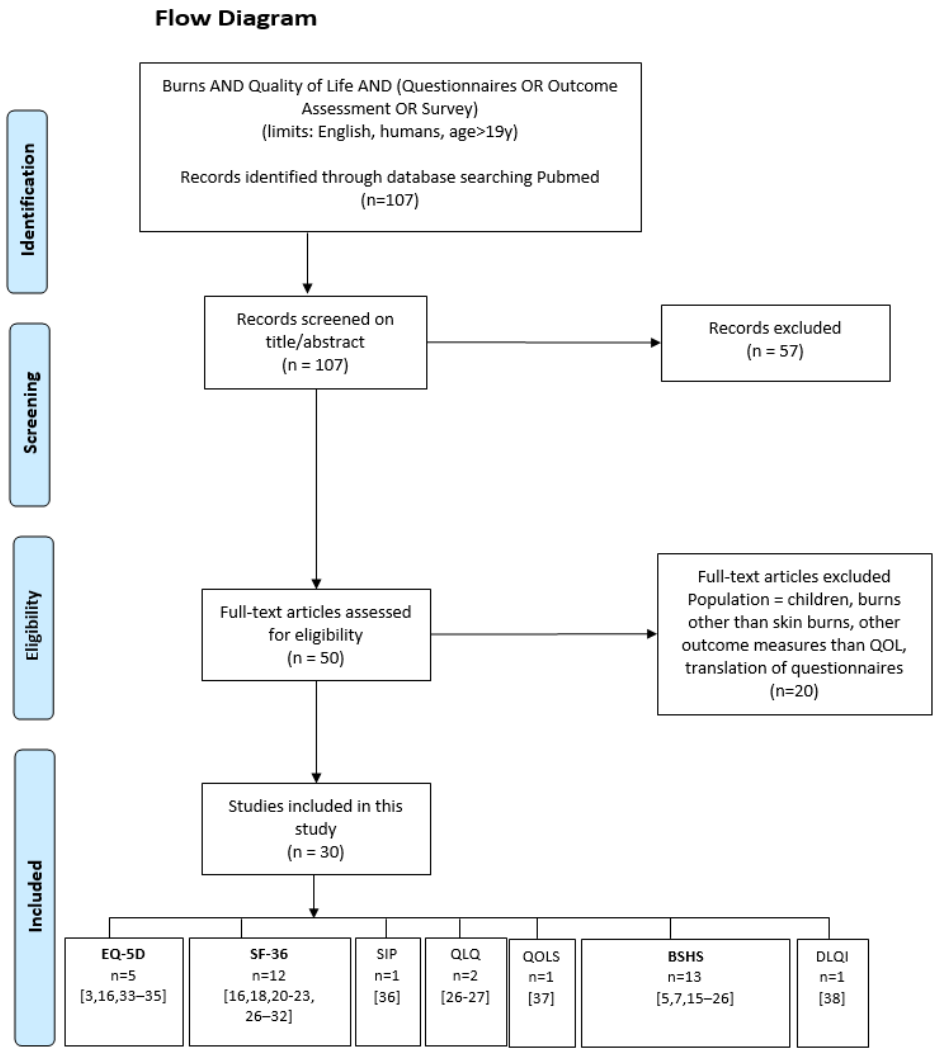

Figure 3-2 Flow diagram of literature search

3.2.2 ICF linkage procedure

A group of four researchers (JM, NVL, KM, UVD) classified the subscales of each quality of life questionnaire into the respective ICF categories: body functions/structures, activity, participation, personal factors or environmental factors. This was done by evaluating/interpreting the items within each subscale of the QOL instruments. The Dutch ICF browser was consulted to establish the decisions[39].

3.2.3 Measures

3.2.3.1 SF-36

The SF-36 (see Appendix) consists of eight subscales; Physical functioning (ten items), Role-physical (four items), Bodily pain (two items), General health (six items), Vitality (four items), Social functioning (two items), Role-emotional (three items) and Mental health (five items)[21,40–43]. Scoring is a two-step process. First precoded numeric values are transformed with a scoring key into values between zero and one hundred (a high score defines a more favourable health status). In the

second step items in the same subscale are averaged together to create the eight scale scores. All subscales of the SF-36 have a fair to good Cronbach's alpha[4,5,20,21,44–48].

3.2.3.2 EQ-5D

The EQ-5D (see Appendix) is a generic assessment tool with five dimensions; Mobility, Self-Care, Usual activities, Pain/discomfort and Anxiety/depression[3,16,49]. Each dimension has 3 levels: no problem, a moderate problem or an extreme problem, yielding many potential combinations of health states across the five dimensions. Finally, subjects rate their overall health on a visual analogue scale from zero (worst imaginable health state) to hundred (best imaginable health state). A domain- related scoring algorithm based on empirical valuations from the UK general population and subsequent statistical modelling is available[3]. Each health status description can be expressed in a summary score. This summary score ranges from one (full health) to zero (for death) and can even have negative values (-.059 as minimum). The summary score can be understood as a measure for the relative desirability of a health status compared with perfect health[3,49].

3.2.3.3 BSHS-B

The BSHS-B is the most recent version of this disease specific tool and has 40 items with nine well defined domains; Heat sensitivity (5 items), Affect (7 items), Hand function (5 items), Treatment regimens (5 items), Work (4 items), Sexuality (3 items), Interpersonal relationships (4 items), Simple abilities (3 items) and Body image (4 items)[9,10,16]. Responses are made on a five point scale from zero (extremely) to four (none/not at all) for each of the 40 items and patients are asked to select the best answer. Mean scores are calculated for each of the domains[50]. All subscales of the BSHS-B have a fair to good Cronbach's alpha[4,5,20,51].

3.3 RESULTS

3.3.1 Comparison of the ICF domains across the questionnaires (horizontal comparison in Table 3-1)

Table 3-1 represents the ICF framework subdomains covered by the respective subscales included into the three questionnaires. The generic scales covered the health condition domains, although the SF-36 provided more different information relative to the EQ-5D, in particular in the body function and the participation domain. Both generic questionnaires excluded contextual factors. The BSHS-B included all health condition domains and personal factors but excluded environmental factors. None of the scales included items on environmental factors and body structures.

3.3.2 Comparison of the subdomains across the questionnaires (vertical comparison in Table 3-1)

In general, subscales addressing impairments in body structures or environmental factors were not included in any of the questionnaires. Regarding the body functions domain there was an overlap between the questionnaires for mental function (see * in Table 3-1). Heat sensitivity and Sexuality were uniquely assessed by the BSHS-B whereas Vitality was uniquely assessed by the SF-36. Regarding the activity domain all three questionnaires showed overlap to some extent. All questionnaires measured physical functioning including aspects of small and gross motor skills (see *** in Table 3-1). The BSHS-B comprised the unique subscale Hand function with focus on fine motor skills of the hands. Within the participation domain all three questionnaires focused on engaging in human interactions (see˜ in Table 3-1). The BSHS-B had a separate subscale e.g., Work. The SF-36 included several participation subscales. All three questionnaires showed an overlap. The contextual factors were not inventoried by the generic questionnaires. The BSHS-B had two unique subscales classified within personal factors: Treatment regimens and Body image.

Table 3-1 Coverage of ICF domains with BSHS-B, SF-36 and EQ-5D.

	Body function/structures (impairments)		**Activity (limitations)**	**Participation Restrictions**	**Contextual factors**		**Others**
	body structures	body functions	Activity	Participation	Personal factors	Environ-mental factors	
BSHS-B subscales		**Heat sensitivity**	**Hand function**	*Interpersonal relationships˜*	**Treatment regimens**		
		Sexuality	*Simple abilities***	*Work˜*	**Body image**		
		*Affect**					
SF-36 subscales		*Mental health**	*Physical functioning****	*Role physical˜*			*General health*
		*Bodily pain***		*Social functioning˜*			
		Vitality		*Role emotional˜*			
				Bodily pain˜			
EQ-5D subscales		*Pain/discomfort***	*Mobility****	*Usual abilities˜*			*General health*
		*Anxiety/depression**	*Self care****				

bolt = unique features for the questionnaire
italic = overlap between questionnaires within ICF domains
*and arrows= illustrating link with other QOL scale

3.4 DISCUSSION

A literature search revealed that the SF-36 and the EQ-5D were the most frequently used generic HRQOL questionnaires in burn-related studies over the last two decades. The BSHS-B version was the only disease specific HRQOL measure available. The subscales of the respective

questionnaires were linked to the ICF domains. In general this classification. revealed that the body function, activity and participation domains were covered by the three questionnaires. Contextual factors were poorly covered and the body structure domain was not addressed. The BSHS-B covered the most domains and it was the only questionnaire that included personal factors (subscales Body image and Treatment regimens).

The content comparison of the three questionnaires revealed considerable overlap across the questionnaires, particularly in the domains body function and activity domains, but some subscales were unique. All three questionnaires comprised mental functions (e.g., Affect, Mental health and Anxiety depression) and both generic measures included pain. The BSHS-B and the EQ-5D comprised two separate subscales for small and gross motor skills whereas both were included in one subscale in the SF-36. However, predominantly lower extremity activities (e.g., walking short and long distances, climbing stairs, kneeling, bending, walking) were measured in the SF-36. The participation domain seemed rather well covered by the questionnaires. However, looking into more detail, not all levels of social interactions were addressed. The SF-36 included interactions with friends, family and work, but the BSHS-B restricted participation to the 'family bond'. The EQ- 5D did not directly address social participation, though it may implicitly be incorporated in the subscale Usual abilities. Considering the unique features of the questionnaires, the BSHS-B included Heat sensitivity and Hand function to measure fine motor skills, Sexuality and Body image whereas the SF-36 had the unique scale Vitality which involved energy and tiredness. Compared with the generic questionnaires, the BSHS-B provided the most burn specific information.

The majority of the subscales concentrate on three domains, while other domains remain untouched. Within the impairments domain, body structures are not addressed. The present findings seem to be consistent with the research of Wasiak et al. who found no concepts linked to body structures within BSHS-B and SF-36. Body structures do not seem primarily relevant for the QOL patient report although care givers do include body structures like skin type, type of surgical intervention (e.g., split thickness graft), upper limb and or lower involvement, etc. in the anamnesis. Considering impairment in body functions, disease specific impairments in body function were lacking in the BSHS-B, for example, pruritus is a common impairment in burn patients and was not addressed in these questionnaires[52–54]. Activity limitations and participation restrictions seem sufficiently covered by the currently used questionnaires. However participation is sometimes narrowly inventoried as described in the paragraph just above. Considering the second part of the ICF framework contextual factors were largely unaddressed. With regards to personal factors only the BSHS-B seems to contribute (including aspects of coping and self image in subscales Body Image and Treatment regimens). Personal factors (e.g., age, gender, coping style, educational level) may

influence functioning as well as QOL, thus implementation within QOL questionnaires seems useful. Although the online ICF browser comprises 30 chapters (including 1424 items that are accompanied by definitions, examples, inclusion and exclusion) no personal factors have been implemented yet[39]. Environmental factors were not addressed in the questionnaires, even though these may have an important impact on burn patients. Social factors (e.g., social care and social and family support) have been recognised as salient to influence coping, prognosis and recovery of patients[55]. The functional outcome of patients with severe burns may need long term adaptation and multidisciplinary care, therefore social factors may be interesting to measure for prognostic reasons. The findings of the current study are consistent with those of Cieza and Stucki (2005) who found that contextual factors are scarcely represented by generic QOL measures[56]. This also accords with earlier observations by Wasiak et al., who showed no concepts linked to contextual factors in the SF-36 and only 2 concepts linked to environmental factors in the BSHS-B. These findings further support the idea to add some items to existing instruments.

Some thoughts on the classification into the different categories of the ICF merit note, as it was not in all cases a straight forward decision because of the subjective nature of this exercise. Within the subscale Heat sensitivity some items inquired about situations they could no longer endure which would at first sight seem to be an activity limitation. However it was the underlying cause (skin is hypersensitive to heat) that was intentioned to measure. Consequently, it was classified within the subscale body function because the skin lost one of its functions. Considering the SF-36 subscale Bodily pain, one part of the questions (pain magnitude) was linked to impairments in body functions, the other part (pain interference) was linked to participation restrictions. These points of discussion provide an explanation as to why this classification partly differs from prior classifications[14,57]. This study showed that in order to comprehensively assess QOL in burn survivors a combination of a disease specific and generic questionnaire is necessary. This finding is in line with earlier recommendations[58]. However even when a combination of the BSHS-B, the SF-36 and the EQ-5D is chosen for QOL assessment some ICF domains remain uncovered. The SF-36 seems complimentary to the BSHS-B and with more focus on the lower extremities and the additional focus on fatigue. The EQ-5D seems feasible when the emphasis is to work quickly because the time to complete is only 5 min[59]. Within the EQ-5D and the BSHS-B vitality was not included, although vitality deficits and fatigue have been found important topics in chronic diseases and might be of interest in this population. Which combination of questionnaires to use should be chosen in light of the study goal, length of the instrument, time to complete and psychometric properties. To cover the unaddressed areas of functioning one needs additional questionnaires (e.g., itch questionnaire, scar scale, participation questionnaires).

In conclusion, from a theoretical view point, this study indicates that on the one hand the currently used instruments overlap regarding several domains and on the other hand they fail to measure domains of functioning that are of interest to patients with burns. An overlap has been empirically confirmed to some extent where prior research has shown correlations between the SF-36 subscales and the BSHS-B[21]. It would be interesting to further explore the ICF linked subscales of the respective questionnaires concerning content overlap on an empirical dataset which might establish or abolish the results of overlap in this study. Regarding the unaddressed domains, it seems inevitable to further develop relevant subscales and add these to existing measures. Adding these domains to existing measures may broaden our understanding of functioning and may more adequately inform clinical practitioners. At the same time, adding more subscales to existing measures would increase the time needed to complete questionnaires, which is an unwanted situation in clinical practice. For screening purposes only, a brief version including the items with the highest distinctive ability for every relevant subscale could assist in overcoming the longer screening time when expanding current measures. Incorporating the unaddressed domains of functioning might be a next challenge in order to fully comprehend the broad spectrum of functioning and QOL following burns.

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4 CONVERGENT AND DISCRIMINANT VALIDITY OF QUALITY OF LIFE MEASURES USED IN BURN POPULATIONS

Meirte J, Van Daele U, Maertens K, Moortgat P, Deleus R, Van Loey N. Convergent and discriminant validity of quality of life measures used in burn populations. Accepted for publication in Burns. doi: 10.1016/j.burns.2016.07.001

Abstract

Introduction: The primary goal of this study was to investigate convergent validity, i.e. overlapping constructs, of the Burn Specific Health Scale-Brief (BSHS-B), the Short Form-36 items Health Survey (SF-36) and the European Quality Of Life Five Dimensions (EQ-5D) within the International Classification of Functioning Disability and Health (ICF) framework. A secondary goal was to examine the discriminant validity of the questionnaires according to burn severity (no surgery versus 1 or more surgeries).

Methods: A prospective multi-centre study in adult patients with burns was conducted. At the 9 months assessment, two generic questionnaires, i.e. the SF-36 and EQ-5D, and the BSHS-B were completed. Pearson correlations were used to evaluate convergent validity. Linear discriminant analysis was used to evaluate discriminant validity.

Results: At 9 months post-burn data from 184 persons were available of which 131 (71%) were male, mean TBSA burned was 11.8% (SD= 10.2). Sixty five (34%) patients did not need surgery, 128 (66%) patients required one or more surgeries. Higher convergence was shown between the generic SF-36 and the condition specific BSHS-B whereas the EQ-5D showed lower convergence with the BSHS-B especially in the domain Activity. The generic scales discriminated across all scales whereas not all BSHS-B scales were able to differentiate problem levels across burn severity groups.

Conclusion: This study demonstrates that the ICF is useful to classify scales in order to identify overlapping areas as well as to uncover gaps in relation to patient reported outcomes. Both the SF-36 and EQ-5D showed the ability to distinguish levels of functioning across burn severity groups. As the BSHS-B performed less well and relevant domains of functioning were not addressed, there is room for improvement and modification of this condition specific questionnaire to better capture burn patients' functioning.

4.1 INTRODUCTION

During the last decade it has been acknowledged that functional outcome is an important parameter of treatment following burn injuries[1]. Functional outcome is often measured using patient reported outcome measures (PROMS). Expert consensus exists on using both generic and disease-specific Quality Of Life (QOL) questionnaires to capture the full impact of a health condition[2]. However, it is insufficiently understood if this combination indeed comprises the full spectrum of functioning as defined by the International Classification of Functioning, Disability and Health (ICF). The ICF is a worldwide used framework to describe the health condition of a patient in a bio-pycho-social context and it can also act as a framework to inventory and compare the content of PROMs[3].

A previous theoretical classification showed the usefulness of the ICF to identify overlap and gaps in scales such as the Burn Specific Health Scale Brief (BSHS-B), the Short Form-36 items (SF-36) and the European Quality of Life 5 Dimensions (EQ-5D)[4]. In general the theoretical classification revealed that the subscales of the three questionnaires covered the Body function, Activity and Participation domains of the ICF. None of the subscales included items on Environmental factors and Body structures. The BSHS-B covered most ICF domains and was the only one to include Personal factors. The content comparison of the three questionnaires revealed considerable overlap across the questionnaires, particularly in the domain Body Function and Activity domains[4]. To our knowledge, there are no studies that empirically evaluate the overlap between generic and disease specific scales within the ICF framework.

Furthermore, it is important to investigate if the scales are able to discriminate between burn severity groups. Discriminant validity is a characteristic of a measure that evaluates the ability to discriminate between groups with known differences. Prior studies[5,6] used total body surface area (TBSA) affected, number of surgeries, or length of stay (LOS) in hospital as burn severity measures. The reliability and validity of the BSHS-B was recently examined in minor burn injuries[7] but it remains unclear how well the different subscales can discriminate between burn severity groups. However, the EQ-5D was sensitive for different levels of burn severity[8]. In a prospective longitudinal study LOS was associated with more problems in all EQ-5Ds dimensions excluding Usual Activities at 3 and 6 months. At 12 months post burn longer LOS was still associated with more problems in Mobility and Pain[8]. The number of surgeries[9] has been shown to negatively affect health related quality of life (HRQOL)[10] and was suggested to outperform somewhat better compared to TBSA as a predictor of long-term HRQOL and speed of recovery[10]. As subscales of PROMs are more often used to identify problem areas in specific health domains[11], it is interesting to evaluate whether the scales are able to detect differences in problem levels in groups that are known to differ from each other.

The aim of this study was twofold: 1) to empirically investigate the overlapping constructs of the BSHS-B, the EQ-5D and the SF-36 within the ICF framework. It was hypothesised that overlapping subscales should show correlations exceeding .50[12,13] and 2) to examine discriminant validity, i.e., how well the scales are able to discriminate between burn severity groups.

4.2 METHODS

4.2.1 Patients

This study was reviewed and approved by the ethics committees of the Martini Hospital, Groningen, The Netherlands, and Ghent University Hospital, Belgium. A prospective multicentre cohort study using the BSHS-B, the SF-36 and EQ-5D to assess QOL 9 months after burn injury was conducted. The results of this study are part of a larger prospective cohort study on psychological problems and quality of life[10, 14]. Adult patients with acute burns admitted to one of six burn centres in the Netherlands and Belgium between March 2003 and April 2005 requiring hospitalisation for at least 72 hours were included in this study. Patients were excluded when they were unable to complete the self-report questionnaires because of poor Dutch proficiency or cognitive disorders. In this study 311 adult burn patients met the inclusion criteria. Fifty-one patients (16%) refused to participate. Informed consent was obtained from 260 patients. We obtained 9 months follow-up data from 184 patients (71%).

4.2.2 Procedure

Eligible patients were invited to participate in the study during hospitalisation. After signing the consent form the first questionnaires were administered during hospitalisation. Once patients left the burn centre follow-up questionnaires were sent by regular mail, including a letter and a prepaid return envelope. Non-responders were reminded within 1 month after the questionnaires were sent. No further efforts were undertaken to collect the measures.

4.2.3 Measures

The BSHS-B, EQ-5D and SF-36 were completed 9 months after the burn injury. The *EQ-5D* is a widely used generic assessment tool which distinguishes five dimensions: Mobility, Self-Care, Usual Activities, Pain/Discomfort and Anxiety/Depression[8, 10, 15]. The EQ-5D covers three domains of the ICF; the domain (impairments in) Body function with subscales Pain/Discomfort and Anxiety/Depression, the Mobility and Self-Care subscales assess Activity (limitations) and Usual Activities inventories Participation (restrictions)[4]. Each dimension or subscale has three response levels: 1= no problems, 2= moderate problems or 3= extreme problems. A Visual Analogue Scale for

General Health can also be part of the EQ-5D but was not included in the analyses of this study. The EQ-5D was translated into more than 60 languages and is used worldwide[8]. The EQ-5D is short and easy to use.

The *SF-36* is a generic measure made up of 36 items that are combined to form eight subscales[16, 17] and covers (impairments in) Body Function with its subscales Mental Health, Vitality and Bodily Pain. Within the ICF domain Activity (limitations) the subscale Physical Functioning was found and the Participation (restriction) domain is covered by multiple subscales: Role-Physical, part of the subscale Bodily Pain, Social Functioning and Role-Emotional[4]. Scoring is a two-step process. Most (29) items responses comprise Likert-type scales (three or six point scales), seven items have a binary response set (1= 0 or 2= 100). Each of the question responses relate to a different pre-coded numeric value. For each of the eight subscales an aggregate percentage score is produced. The percentage scores range from 0% (lowest or worst possible level of functioning) to 100% (highest or best possible level of functioning). In the second step scores are averaged across items constituting a scale[18, 19].

The *BSHS-Brief (BSHS-B)* is the most recent version of this burn specific instrument. It includes 40 items comprising 9 domains[20, 21], covering each domain of the ICF framework. Heat sensitivity, Sexuality and Affect comprised Body Function, Hand Function and Simple Abilities measure Activity limitations, Work and Interpersonal Relationship cover the domain Participation and Treatment Regimens and Body Image assess Contextual Factors[19]. Item responses are scored on a 5-point scale ranging from 0 (= all the time/great difficulty) to 4 (= never/no difficulty). Mean scores are calculated for each subscale and high scores indicate a good perceived health status[4].

4.2.4 Statistical analysis

Construct validity was examined using a priori hypotheses for discriminant and convergent properties of the instrument. Convergent validity refers to how well subscales correlate with other measures that are assumed to be related. Convergent validity, assessing the overlap between measures, was investigated using Pearson correlation coefficients among different subscales[12, 22]. The degree of correlations are outlined as follows: small 0.10 to 0.29, moderate ≥0.30 to 0.49 and strong ≥0.50[23]. We hypothesized that subscales of the EQ-5D, the SF-36 and the BSHS-B theoretically classified as overlapping, were highly correlated (Table 3-1). Strong correlations indicate that the subscales assess similar constructs[12].

Discriminant validity evaluates the ability to discriminate between groups with known differences[24]. In this study discriminant validity was assessed by comparing two groups: those

requiring no surgery versus those requiring ≥1 surgery. To describe discriminant validity a linear discriminant analysis was used to determine classification capacity of the different subscales of the SF-36, EQ-5D and BSHS-B in the two predefined groups (no surgery versus ≥1 surgery). In the analysis Box's M analysis for evaluation of equality of covariances and calculation of correctly predicted classification or hit ratio were included. Statistical significance was considered if $p < .05$. Analysis were performed using SPSS 20.0.

4.3 RESULTS

4.3.1 Demographic and clinical characteristics of patients

A total of 184 participants completed the 9 month assessment of which 131 (71%) were male and 53 (29%) were female. Participants were on average 39.0 years old (SD= 12.8). The mean TBSA was 11.8% (SD= 10.2). The mean LOS in hospital was 23.0 days (SD= 21.0). The median number of surgeries was 1 (ranging between 0 and 16, SD= 1.8). Sixty five (34%) patients did not need surgery, 128 (66%) patients required one or more surgeries.

4.3.2 Convergent validity between BSHS-B, EQ-5D and SF-36 subscales.

Correlations between the subscales of the BSHS-B and the EQ-5D are shown in the upper part of Table 4-1. The negative correlations reflect a high score on an EQ-5D subscale as indicative of poor health state while a high score on the BSHS-B subscale is indicative of better health. Only two correlations exceeded .50. Within the Body Function domain, Affect (r = -0.69) was most strongly related with Anxiety/ Depression. Within the Participation domain, Work (BSHS-B) and Usual Abilities (EQ-5D) revealed a strong (r=-0.63) correlation. Correlations within the Activity domain across the questionnaires were low.

Correlations between the subscales of BSHS-B and the SF-36 as categorised within the ICF domains are shown in the lower part of Table 4-1. High scores on the SF-36 and BSHS-B reflect a good health state. Again, within Body function, the Affect subscales were strongly related (r=-0.67) and within the Participation domain several high correlations were observed, with Work and Role Physical showing the highest correlation. Within the Activity domain, Physical Functioning and Hand Function were related.

When comparing the overlap between the two generic scales, the theoretically assumed overlap was confirmed by correlations exceeding 0.50. Only one correlation was lower, Role Emotional and Usual Activities. Correlations are shown in Table 4-2.

The highest correlations were indeed observed between subscales that were classified within the same ICF domain. However, other significant correlations appeared, providing insight in how domains are inter-connected. A combination of the scales provides additional insight in problem areas.

Table 4-1 Pearson correlations between subscales of the BSHS-B the EQ-5D and the SF-36

	ICF domain	**Body function**			**Activity**		**Participation**		**Contextual factors**	
	BSHS-B	Affect	Sexuality	Heat Sensitivity	Simple Abilities	Hand Function	Work	Inter. Relat.	Body Image	Treatment Regimens
ICF domain	**EQ-5D**	r	r	r	r	r	r	r	r	r
Body Function	Anxiety/ Depression	-0.69	-0.48	-0.36	-0.41	-0.33	-0.40	-0.41	-0.54	-0.45
	Pain/ Discomfort	-0.37	-0.38	-0.39			-0.50		-0.48	-0.46
Activity	Mobility				-0.28	-0.30	-0.40			
	Self-Care				-0. 34		-0.34			
Participation	Usual Activities		-0.33	-0.38	-0.32	-0.32	-0.63	-0.12	-0.38	-0.37
	SF-36									
Body Function	Mental Health	0.67	0.49	0.36			0.47	0.37	0.54	0.42
	Vitality	0.56	0.44	0.36	0.37	0.34	0.51	0.38	0.50	0.40
	Pain (also part Participation)	0.44	0.47	0.42	0.42	0.40	0.60	0.26	0.53	0.55
Activity	Physical Functioning	0.40	0.42		0. 50	0.50	0.59		0.41	0.46
Participation	Social Functioning	0.60	0.50	0.37	0.36	0.33	0.59	0.31	0.56	0.53
	Role Physical	0.48	0.43	0.40	0.43	0.44	0.70	0.18	0.42	0.47
	Role Emotional	0.47	0.37		0.32		0.45	0.16	0.45	0.40

Number of observations between 172 and 182

r= Pearson correlation

Only correlations exceeding .30 are presented excluding those that were hypothesized to be high as marked by the squares.

Correlations are all significant at the .05 level

= theoretically assumed overlap

Table 4-2 Pearson correlations between subscales of the EQ-5D and the SF-36

	ICF domain	**Body function**			**Activity**	**Participation**		
	SF-36	Mental Health	Vitality	Pain (also part Participation)	Physical Functioning	Social Functioning	Role Physical	Role Emotional
ICF domain	**EQ-5D**	r	R	r	r	r	r	r
Body Function	Anxiety/Depression	-0.67	-0.54	-0.42	-0.33	-0.63	-0.42	-0.57
	Pain/Discomfort	-0.39	-0.39	-0. 72	-0.43	-0.48	-0.50	-0.44
Activity	Mobility			-0.38	-0.67	-0.30	-0.41	
	Self-Care			-0.45	-0.64	-0.37	-0.30	
Participation	Usual Activities	-0.38	-0.42	-0.55	-0.59	-0.52	-0. 68	-0.46

Number of observations between 177 and 179

r= Pearson correlation

Only correlations exceeding .30 are presented excluding those that were hypothesized to be high as marked by the squares.

Correlations are all significant at the .05 level

= theoretically assumed overlap

4.3.3 Discriminant validity of the HRQOL subscales between burn severity groups

Table 4-3 presents the mean scores for the BSHS-B for the two severity groups. A higher problem level was found in the ≥ 1-surgery group. However the differences between the severity groups in the subscales Affect, Heat Sensitivity, Simple Abilities, Hand Function and Interpersonal Relationship did not reach statistical significance. The largest differences between groups were found with respect to Work, Body Image and Treatment Regimens. When tested by Box's M the subscale Work showed a significant unequal covariance between both groups and should be interpreted with caution. The cross validated classification showed that overall between 69.4 and 69.8% was correctly classified, this is shown in Table 4-3 as the discriminant analysis (DA) hit ratio.

Regarding the mean EQ-5D subscale all domains showed a statistically significantly higher problem level in the ≥1-surgery group. Both groups presented the most difficulties in the subscales Pain/Discomfort, Anxiety/Depression and Usual Activities, as shown in Table 4-4. Figure 4-1 shows the problem levels of the five dimensions. When tested by Box's M the following subscales showed a significant unequal covariance between both groups and should be interpreted with caution; Mobility, Self-Care and Usual Activities. The cross validated classification showed that overall between 69.7 and 70.1% was correctly classified.

The SF-36 subscales were also able to discriminate across severity groups (Table 4-5). In the no-surgery group lowest scores were found in the impairments in the subscales Vitality and Mental Health and for the ≥1-surgery group lowest scores were found in subscales Vitality and Mental Health as well as Role Physical and Role Emotional at 9 months post injury. All subscales detected statistically significant differences between the severity groups. When tested by Box's M the subscales Physical functioning and Social functioning showed a significant unequal covariance between the groups. The cross validated classification showed that overall between 68.2 and 71.7% was correctly classified.

Table 4-3 Discriminant validity of the BSHS-B subscales

	BSHS-B	no-surgery N = 56	≥1 surgery N = 128	P value	DA hit ratio %
		mean (SD)	mean (SD)		
ICF domain					
Body Function	Affect	3.65 (0.69)	3.43 (0.81)	0.07	69.6
	Sexuality	3.82 (0.61)	3.51 (0.82)	0.01*	69.4
	Heat Sensitivity	3.03 (0.92)	2.78 (0.96)	0.10	69.4
Activity	Simple Abilities	3.88 (0.59)	3.69 (0.68)	0.07	69.6
	Hand Function	3.84 (0.61)	3.65 (0.80)	0.07	69.6
Participation	Work	3.67 (0.70)	3.11 (1.15)	0.00*	69.8
	Interpersonal Relationships	3.87 (0.55)	3.77 (0.56)	0.30	69.6
Contextual Factors	Body Image	4.59 (1.08)	3.81 (1.45)	0.00*	69.4
	Treatment Regimens	3.68 (0.71)	3.29 (0.96)	0.00*	69.4

N= number of patients, SD= standard deviation, P value= investigation of mean difference between groups *= $p < 0.05$, DA hit ratio= Discriminant analysis hit ratio (% correctly classified)

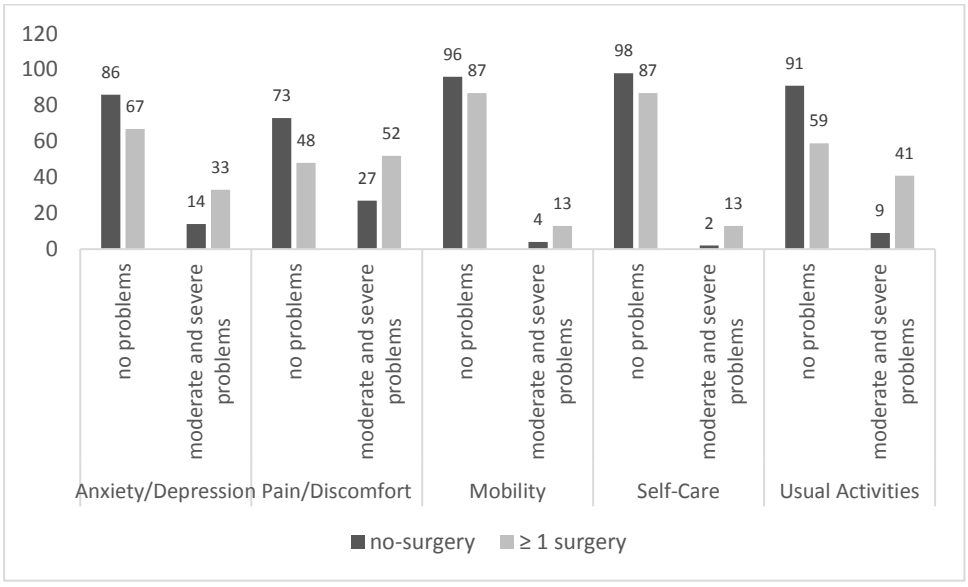

Figure 4-1 Distribution of the responses in the no-surgery group and ≥1 surgery group to the items of the EQ-5D at 9 months

Tabel 4-4 Discriminant validity of the EQ-5D

	EQ-5D	no-surgery N = 56	≥1 surgery N =129	P value	DA hit ratio %
ICF domain		**mean (SD)**	**mean (SD)**		
Body function	Pain/Discomfort	0.27 (0.45)	0.55 (0.56)	0.00*	69.7
	Anxiety/Depression	0.15 (0.36)	0.36 (0.54)	0.01*	70.1
Activity	Mobility	0.04 (0.19)	0.14 (0.37)	0.05*	70.1
	Self-Care	0.02 (0.13)	0.16 (0.41)	0.01*	69.7
Participation	Usual Activities	0.09 (0.29)	0.43 (0.54)	0.00*	69.7

N= number of patients, SD= standard deviation, P value= investigation of mean difference between groups, *= $p < 0.05$, DA hit ratio= Discriminant analysis hit ratio (% correctly classified)

Table 4-5 Discriminant validity of the SF-36

	SF-36	no- surgery N = 57	≥1 surgery N = 123	P value	DA hit ratio%
ICF domain		**mean (SD)**	**mean (SD)**		
Body Function	Mental Health	79.77 (15.81)	70.26 (21.55)	0.00*	68.3
	Vitality	75.20 (17.53)	63.06 (19.83)	0.00*	71.7
	Pain	86.68 (18.16)	75.51 (23.29)	0.00*	68.3
Activity	Physical Functioning	94.39 (13.06)	81.95 (21.31)	0.00*	68.3
Participation	Social Functioning	92.32 (15.08)	77.34 (25.02)	0.00*	68.3
	Role Physical	84.65 (27.85)	59.84 (40.98)	0.00*	68.2
	Role Emotional	85.38 (29.56)	67.62 (42.01)	0.01*	68.2

N= number of patients, SD= standard deviation, P value= investigation of mean difference between groups, *= $p < 0.05$, DA hit ratio= Discriminant analysis hit ratio (% correctly classified)

4.4 DISCUSSION

The present study empirically demonstrates the convergence between the generic EQ-5D and SF-36 and the BSHS-B on subscale level in line with a prior theoretical classification within the ICF framework[4]. The convergence between the two generic scales was stronger than the overlap with the burn specific scale, as reflected by higher correlation coefficients across the subscales. Furthermore, the correlations between the SF-36 and BSHS-B were on average higher as compared to those found in the EQ-5D – BSHS-B comparison. This study also elucidated underlying relationships between domains that provide insight which burn specific domains affect the generic domains of functioning. Furthermore, the results of this study suggest that the generic questionnaires outperform the BSHS-B regarding the ability to differentiate problem levels between burn severity groups. Further study may be required to establish the nature of these differences, i.e., if these differences are a true reflection of the situation (hand function may be affected in only a subsample of the patients that needed surgery) or whether it is due to the lack of sensitivity of the scale.

This study supports significant content overlap in the generic scales as hypothesized in a prior study using the ICF as the leading framework[4]. Our results are in line with those of Öster et al.[8] in which the EQ-5D index and Visual Analogue Scale (VAS) scores correlated well with all SF-36 subscales ranging between 0.55 and 0.78 suggesting that similar constructs of HRQOL were measured. Moreover, the correlations between the scales provided insight into underlying problem areas for example, Vitality showed higher correlations with psychological domains such as Anxiety/Depression (EQ-5D) as compared to physical domains suggesting that psychological problems largely affected vitality. Another example relates to Usual Activities (EQ-5D) that was stronger related to SF-36 subscale Physical Functioning relative to psychological functioning. This provides valuable insight into underlying problem areas.

The overlap between the EQ-5D and BSHS-B was modest. Only two out of five hypothesized overlapping subscales showed correlations exceeding 0.50, i.e. Anxiety/Depression – Affect and Usual Activities – Work. These results support previous research that showed comparably low associations between BSHS-B subscales and EQ-5D index at 6 and 12 months post burn injury[8]. Especially Hand Function and Sexuality respectively showed low correlations with the EQ-5D index and those subscales were relatively independent to other reported health related problems[25]. The findings in this study suggest that both questionnaires measure different components of HRQOL and seem complementary to a large extent. Despite its briefness, the EQ-5D was well able to discriminate between severity groups and supports its usefulness in burn populations.

Somewhat stronger associations were found between the subscales of the SF-36 and the BSHS-B. This supports the previously demonstrated validity of the SF-36 in burn populations[16]. The BSHS-B subscale Work was strongly associated with several SF-36 subscales in different domains of functioning and showed lower associations with psychological symptoms as was also reported in a prior study[17]. In contrast to earlier findings, however, no evidence of high associations between Heat Sensitivity, Treatment Regimens and Body Image (domain Skin involvement) and role concerns (Social Functioning, Vitality and Mental Health) was detected[17]. The lower associations between appearance related problems and social difficulties in our study may be explained by the lower mean TBSA burned in this group of patients. Contextual factors comprised by the subscales Treatment Regimens and Body Image of the BSHS-showed relatively high associations with other ICF domains. This is not that surprising as Contextual Factors are known to influence (facilitate or hinder) all components of functioning[1, 26, 27].

This study suggests that the generic scales were better able to discriminate problem levels across burn severity as five out of nine BSHS-B subscales (Affect, Heat Sensitivity, Simple Abilities, Hand Function and Interpersonal Relations) did not strongly discriminate between these groups. The finding that affect was more severely disturbed according to the generic scales in the more severely burned group (with subscales Anxiety/Depression in EQ-5D and Mental Health in SF-36) underscores the lower sensitivity in the BSHS-B. These results also support previous findings which reported a superior sensitivity of the SF-36 subscales compared to the BSHS-B over time[16]. However, one could argue that problem levels in some of the scales may have been too small to detect differences across the severity groups. For example Hand function will be affected only in persons with hand burns which will not necessarily be true in all respondents in the more severe burn group. On the other hand, the generic measures may be too broad, also including pre-existing health problems that may have little to do with the burn injury. Other study methods, e.g., qualitative approaches may be needed to elucidate this issue. Furthermore the short version of the BSHS was used in this study. Longer versions such as the BSHS-Revised (BSHS-R) or the BSHS-Abbreviated (BSHS-A) may score differently on sensitivity.

For use in clinical practice ideally there should be minimal overlap between generic and disease specific instruments to lower the cost of scoring of a number of different measures. However, it is also important to measure all relevant areas of functioning to capture the full impact of a condition. This may add another layer of decision-making and complexity when measuring HRQOL for clinical purposes. This study showed that according to the ICF framework, applying both generic and condition specific measures, did not address the full scope of problems following burn injury. None of the generic scales includes Body Structure and other relevant impairment in Body

Function (e.g., itch or stigma, coping). Whilst personal factors can be found in the BSHS-B in the subscale Treatment Regimens and Body Image, but this is still limited. Personal factors may include various aspects such as gender, race, age, coping styles, education, profession, past and current experience, individual psychological assets and other health conditions, all of which can affect health and functioning[27].As illustrated in this study, problems in the participation area were associated with both physical and social problems but the BSHS-B did not make the underlying problems explicit. For example stigmatisation may be an underlying problem[26]. These findings indicate there is room for improvement regarding the burn specific instrument both in defining necessary problem areas of functioning currently not included as well as a critical reflection on domains that add little information from a clinical perspective (e.g., treatment regime). In summary, despite the burden to the patient and the clinician it seems necessary to combine a generic measure and a condition specific measure as they are complementary but still incomplete. New technologies such as computerized testing can help limit the burden of duplication in the future[11, 29].

Some limitations merit note. This study was part of a larger study design that required patients with adequate cognitive functioning. Older patients and those suffering from cognitive disorders were not included while these patients might have had worse HRQOL. Proxy assessment of HRQOL in those with mental and cognitive problems would be an alternative for self-reports and should be considered in future studies[2]. In addition persons who were lost to follow-up were statistically younger and may have had a better quality of life. The impact of these biases may limit generalization to the general burn population. The time frame chosen to compare the questionnaires may have influenced the results, as more problems may be experienced at earlier time points. Furthermore, there was a sample size difference between the no surgery and the ≥ 1 surgery group and the measures slightly differ in their timeframe; the EQ-5D examines current health status, the SF-36 uses a 4 week period and the BSHS-B does not specify the timeframe. The sample and timeframe differences may have affected the accuracy of the comparison.

4.5 CONCLUSION

The results of this study illustrate that the ICF framework is useful to classify scales in order to identify overlapping areas. Scales that are largely overlapping unnecessarily increase the burden and should be avoided. The psychometric assessment of the relationship between the EQ-5D, the SF-36 and the BSHS-B shows that convergence is higher between the generic measures (EQ-5D and SF-36) as compared to the BSHS-B. Both generic scales performed well regarding discriminant

validity. Additionally, the ICF framework previously appeared useful to identify gaps regarding domains that are currently overlooked. Consequently, there is room for improvement, particularly regarding the burn-specific measure. This study also illustrated that a short generic scale such as the EQ-5D can provide interesting information but should be combined with a more comprehensive condition-specific scale in order to capture the full impact. Of notice, the use of a coherent timeframe across the scales should be considered to better attune the measurements. Overall, this study supports the view that currently the most frequently used scales to measure functioning fall short to measure the full impact of a burn injury.

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Part 2
Vacuum massage

In Part 2 we elaborate on the effects of vacuum massage. It consists of 2 chapters. Chapter 5 is a comparative study between a usual care group and an intervention group receiving vacuum massage in addition to the usual care and elaborates on the observed effects for pain, pruritus and TPT. Chapter 6 focusses on the effects of vacuum massage on epidermal and dermal structures observed with echographic images and its relation to mechanotherapy.

5 THE EFFECTS OF VACUUM MASSAGE ON PAIN, ITCH AND SENSORY PERCEPTION IN BURN SCARS: A COMPARATIVE STUDY

In preparation

Abstract

The adult burn population with burn scars frequently report pruritus, pain and loss of sensation due to scarring. These impairments in functioning have an important impact and inhibiting factor on daily activities. Pain, itch and paresthesia in combination with applied noninvasive treatment modalities remain poorly documented in the aftercare setting for burn patients. Although vacuum massage was invented to treat burn scars only limited A1 publications describe its efficacy.

The main objective of this study was to investigate the effect of vacuum massage on pain, itch and Touch Pressure Threshold (TPT) in burn scars.

Pain and pruritus were examined with the Patient Scar Assessment Scale. Loss in cutaneous sensation was measured with an aesthesiometer to determine TPT. Thirty two burn scars were treated with standard of care (usual care group) and 30 burn scars were treated with vacuum massage (intervention group) in addition to the usual care. Both groups were comparable at baseline on several clinical factors. Data were registered at baseline, after 1, 3 and 6 months, and again after 1 year.

The results of this study did not detect evidence that vacuum massage is the preferred additional treatment to improve pain or itch. The between group analyses revealed that there were no statistically significant differences between the groups over time. The intervention group showed statistically significant improvement over time for pain after corrections for baseline value and scar age but showed no improvement over time for itch. However the most obvious finding to emerge from the analysis in the intervention group is the statistically significant improvement for TPT with statistically significant lower mean values for the intervention group at 3 months and 1 year.

These findings show that when treating burn scars with diminished sensation vacuum massage may be a valuable additive.

5.1 INTRODUCTION

A variety of noninvasive treatments for burn scars have been described in recent literature like pressure therapy, hydration, silicon gels, massage therapy, mobilisation and vacuum massage[1]. Vacuum massage or depressomassage or Endermology ® is a noninvasive massage technique using a mechanical device that lifts the skin by means of suction creating a skin fold[2–5].

Although vacuum massage was originally intended to treat burns and scars[5] very few A1 publications describe its physiological effects. Two articles found a decrease in pain and itch[6,7], however the population was not burn- or scar- specific. In one study patients with radiation induced skin fibrosis were treated[6] and in another study the population consisted of people treated for morphea, a rare skin condition that causes isolated patches of hardened skin[7]. In the latter no control group was evaluated and no significant changes were reported[4]. The literature on vacuum massage shows evidence of collagen restructuring and reorientation and a positive correlation between the numbers of treatments and the efficacy of the treatment[2,3,8]. In general the methodological quality of the studies was poor and more comparative trials are required. In contrast to vacuum massage, the effects of manual massage on burn scars have been investigated and have shown positive effects on the reduction of pain[9,10] and itch[10–12]. To our knowledge the effects of massage therapy on the sensory function of the skin have not yet been explored. While some research has been carried out on the effects of manual massage no studies exist which explored the efficacy of vacuum massage on hypertrophic burn scars.

After a thermal injury 36% of the individuals complain of pain, 72 % report paresthetic sensations and more than half of the patient experience every week sensory problems that interfere with activities of daily living[13]. This decreased sensory function might be caused by diminished nerve fiber function in the scar, changes in the central nervous system's perception of stimuli or changes in the tissue structure, such as decreased pliability[14]. Even in minor burn scars reduced sensory function is observed[15]. Tactile sense of touch or light touch can be examined with the Touch Pressure Threshold (TPT) method using the Semmes Weinstein Monofilament Test (SWMT)[13,16–18]. Besides sensory problems pain and itch are common physiological consequences of burns. Between 16 and 87% of the individuals with burns suffer from itching[19]. Itch is mainly caused by a higher release of histamine and or elevated sensitivity in the sensory nerves to the release of histamine. Pain and stiffness of a scar are more related to the collagen and elastin fibres. Elastin fibres are thinner or not present in scarred tissue and collagen fibres are thinner and more densely packed compared to in normal skin[20]. Pain and itch are supposed to be interrelated in scars[19], however in a recent study no correlations were shown between pain and itch. Pain appeared to be correlated to the thin and dense collagen fibres. There is an obvious differentiation between the neurons involved in the

creation of itch and pain, at least in the peripheral regions[21]. Provocation of pain and itch in the periphery area of the scar suggests that a strong stimulus induces the dermal unmyelinated afferent C-fibres, resulting in pain sensations; a weaker stimulus induces the epidermal unmyelinated afferent C-fibres, resulting in itch sensations[20]. Pain and itch can be assessed with subjective questionnaires or scar scales[22,23]. The items pain and pruritus are typical neurological sensations of a scar[24] and it has been described that the patients assess pain and pruritus as the most severe symptoms in relation to their scar[24]. The aim of this study was to investigate the effect of vacuum massage on pain, itch and TPT in hypertrophic burn scars.

5.2 Material and Methods

5.2.1 Study design, subjects, intervention

This study was a non-randomised controlled trial and reports the observed effects of vacuum massage compared to standard of care on pain, itch and TPT. Data were collected between February 2009 and May 2014 in Oscare, Organisation for Burns, Scar Aftercare and Research, Antwerp, Belgium. Patients were allocated into 2 groups, an intervention group and a usual care group (control group) based on the possibility and willingness of the patients to come to the Oscare centre for their vacuum massage treatment. All the patients received usual care therapy (e.g., pressure garments, silicone gels, hydration) and physical therapy (e.g., manual physiotherapeutic techniques, massage therapy) as described by a physician. The intervention group additionally received vacuum massage (mechanical massage therapy using a suction device) during 6 months. Therapist and assessors were not blinded and aware of treatment allocation.

Patients of at least 18 years of age with scars resulting from burn injuries with full epithelialisation were eligible for this study. This study was approved by the Ethics Committee of ZNA campus, Antwerp (4130). Informed consent was obtained from all patients. In total 60 patients with burn scars (from both groups) were analysed in this study, the flow diagram of patient recruitment is shown in Figure 5-1. All patients agreed to participate in this comparative clinical trial. Thirty seven scars (comprising 35 patients since 2 patients were evaluated for 2 scar locations) were allocated to the intervention group and 53 scars were allocated to the usual care group.

In total 90 scars were measured. The boundaries of the test sites were carefully marked out, captured on a digital picture and referred to during each visit for defining exact (re)location for assessment. Twenty three patients of the usual care group dropped-out since they didn't want to

complete the study. Five patients were lost for the intervention study. The intervention group comprised 32 scars (28 patients with a single tested scar location and 2 patients tested on 2 locations) and 30 scars from 30 patients formed the usual care group.

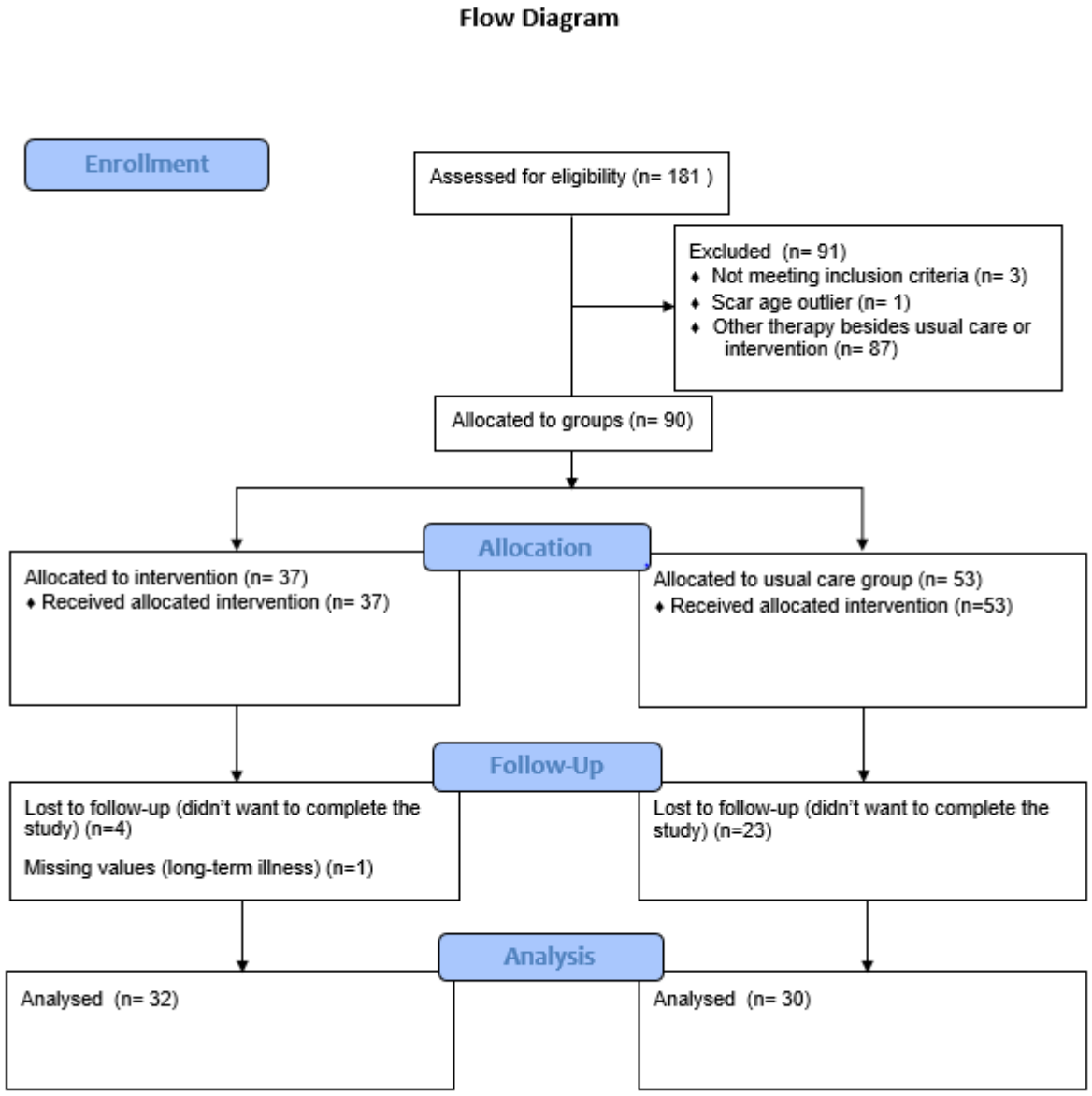

Figure 5-1 Flow diagram for patient recruitment

n= number of scars

Patients in the intervention group were treated during a period of 6 months with the PRUS® vacuum massage device (Figure 5-2). The first 3 months after the first assessment patients of the intervention group were treated 2 to 3 times a week (at least 10 treatments per month). The following 3 months frequency was decreased to only once a week. After 6 months the treatment with the vacuum massage was stopped. Depending on the skinfold thickness the applied suction

pressure varied between 250 and 900 mbar depending on location and scar thickness. The duration of a treatment was 5 minutes per 10cm² (view Table 5-1). All patients continued the usual physical therapy and scar care which included pressure garments, silicone gels, manual physiotherapeutic techniques, massage therapy according to the techniques of D. Jaudoin et al[25], hydration as prescribed by the referring medical specialist. The usual care group received the physical therapy within Oscare or outside the centre in private physical therapy practices.

Figure 5-2 PRUS vacuum massage device

Table 5-1 Treatment protocol for the vacuum massage treatment in the intervention group

	Settings	
treatment frequency 0-3 months	10/month	
treatment frequency 3-6 months	1/week	
treatment duration/10 cm²	5 min	
suction power	250-900 mb	depending on skin fold thickness
pulsation frequency	0.25-0.50 Hz	suction – no suction
treatment heads Ø	6 – 28 mm	depending on location of scar

5.2.2 Measures, protocol

To stabilise cutaneous blood flow, all patients were asked to remove pressure garments at least 30 minutes before measurements were started. Measurements were performed before the treatment was executed. Patients of both groups were evaluated at baseline before the first treatment (T0), after 1 month (T1), 3 months (T2), 6 months (T3) and 1 year (T4).

The outcome measures pain and itch were registered with 2 items of the POSAS questionnaire (Patient scale/pain; Patient scale/itch). The POSAS is the preferable scar scale to assess patient's perspective of the scar[22], it consists of a six-item scale based on clinically relevant scar characteristics[26] which is scored on a 10-point rating scale[24] and has good clinimetric properties[24]. The intensity of pain and itch is assessed on a 10 point visual analogue scale. One is defined as no complaints and 10 is the worst imaginable complaints. TPT was measured to evaluate the recovery of the sensory function of the skin using the SWMT with the ascending descending procedure[16].The higher the value for TPT the more rigid and thick the filaments were hence meaning the less sensitive the scar is to touch.

5.2.3 Statistical analysis

Statistical analysis was performed with SPSS 20 software for Windows (IBM, Armonk, New York, USA). Means and 95% confidence intervals were obtained from a general linear model for longitudinal measurements and the repeated measures over time. Demographics standard descriptive statistics including means, standard deviations and ranges were used to summarise patient demographic and presentation data including age, gender, aetiology, area and location of treatment site. A mixed ANOVA procedure was used to determine an interaction between time and intervention on the dependent variables. For the between-group analysis a two-way ANOVA was carried out with the intervention being the between-subjects factor. The evolution over time is evaluated on all repeated measures. The post-baseline values (at T1, T2, T3 and T4) are compared between groups with baseline values and scar age being covariates, allowed to vary over time. For the within-group analysis a repeated measures ANOVA was carried out with time being the within-subjects factor. The Bonferroni post hoc test with pairwise comparisons was used to determine statistically significant differences between the different time-points. Estimates of effect size are also reported. Statistical significance was set at $p < .05$.

5.3 RESULTS

5.3.1 Demographic and clinical characteristics of patients

A total of 62 scars comprised 38 men and 24 women. The intervention or vacuum massage group comprised 23 men and 9 women, while in the usual care group 15 men and 15 women were treated. For the intervention group the mean age of the group was 40.25 (SD= 13.27) years old. Scar age was 14.40 (SD= 13.68) months and 18 patients had spontaneous healing of their scars, while 14 required split thickness skin grafts. The mean age for the usual care group was 44 (SD= 18.47) years, scar age was 14.40 (SD= 22.80) months and 14 subjects healed spontaneously while 16 had skin grafts for their burn injuries. (Table 5-2)

Table 5-2 Demographics and clinical characteristics of patients

	Usual care group n=30	**Vacuum massage group** n=32
Gender % Male: Female	50:50	72:28
Mean age in years (range, SD)	44 (18-65, 18.47)	40.25 (18-64, 13.27)
Mean scar age in months (range, SD)	14.40 (1-93, 22.80)	14.40 (3-58, 13.68)
Spontaneous healing %	47	56
Split thickness skin graft %	53	44
Skin type Caucasian: Asian: North African	27:3:0	30:0:2

n, number of participants, %, percentage, SD, standard deviation

Baseline measurements for pain, itch and TPT for both groups are presented in Table 5-3. There were no statistically significant differences between the groups at baseline for pain, itch and TPT.

Table 5-3 Mean values for POSAS pain, POSAS itch and TPT at the different time points

	T0				T1				T2				T3				T4			
	mean	SD	95%CI		mean	SD	95%CI		mean	SD	95%CI		mean	SD	95%CI		mean	SD	95%CI	
Pain			LB	UB			LB	UB			LB	UB			LB	UB			LB	UB
Usual care group	3.43	2.73	2.42	4.45	3.27	2.63	2.29	4.25	2.97	2.48	2.04	3.89	2.57	2.16	1.76	3.37	2	1.91	1.29	2.71
Intervention group	2.41	2	1.69	3.13	2.22	1.24	1.77	2.66	2	1.32	1.52	2.48	1.87	1.62	1.29	2.46	1.56	1.08	1.18	1.95
Itch																				
Usual care group	3.43	0.42	2.59	4.28	3.3	0.42	2.45	4.15	3.2	0.38	2.43	3.97	2.1	0.42	1.27	2.94	2.3	0.36	1.59	3.01
Intervention group	3.69	0.41	2.87	4.5	3.47	0.41	2.65	4.29	3.06	0.37	2.32	3.81	2.69	0.4	2.16	3.78	2.66	0.35	1.97	3.35
TPT																				
Usual care group	4.89	0.94	4.53	5.26	4.69	0.94	4.32	5.05	4.75	0.81	4.44	5.06	4.64	0.85	4.31	4.97	4.72	0.83	0.44	5.04
Intervention group	4.92	0.61	4.7	5.14	4.64	0.55	4.45	4.84	4.6	0.51	4.41	4.78	4.49	0.5	4.3	4.66	4.48	0.53	4.29	4.68

T0= baseline T1= 1 months T2= 3months T3= 6 months T4= 1 year SD= standard deviation CI= Confidence Interval %= percentage LB= Lower bound UB= Upper Bound

5.3.2 The change in pain scores

In the between group analysis the ANOVA detected no statistically significant interaction between the intervention and time for pain. This was confirmed for the different post-baseline values after corrections for scar age and baseline value.

For the total population the main effect of time showed a statistically significant difference at the different time points (p= 0.000). Post hoc analysis showed that this significant difference was only reached after 1 year (p= 0.001) compared to baseline.

In the within group analysis the usual care group showed a statistically significant improvement (p= 0.01) over time and post hoc analysis revealed that this improvement was reached after 1 year compared to baseline (p= 0.011) with a moderate effect size (d=0.62). The intervention group showed no significant improvement over time (p= 0.058). Note however that after corrections for scar age and baseline value -analysis with transformed data- both groups showed a statistically significant improvement over time (control p= 0.003, intervention p= 0.017). These results are illustrated in Figure 5-3.

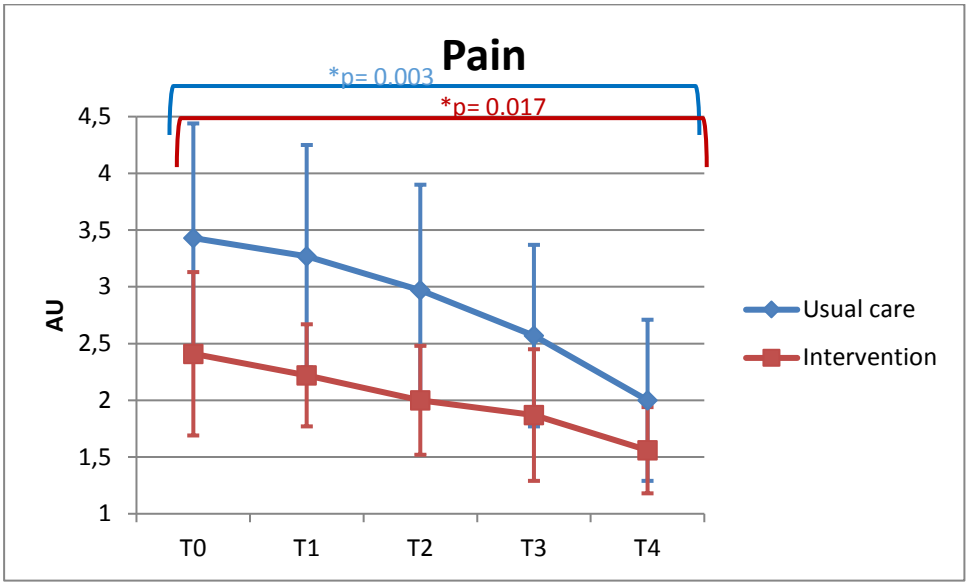

Figure 5-3 Line charts of the pain scores (with confidence interval) in the control group and the intervention group at the different time points

*These results are after correction for scar age and baseline values. The statistically significant improvement over time is illustrated with *****.*

5.3.3 The change in itch

The between group analysis showed no significant difference in intervention effect on itch over time between both groups. This was confirmed for the different post-baseline values after corrections for scar age and baseline value.

For the total population the main effect of time showed a statistically significantly difference at the different time points (p< 0.005). Post hoc analysis showed that this significant difference was reached after 6 months compared to baseline (p= 0.02).

In the within group analysis over time (as illustrated in Figure 5-4) the usual care group showed a statistically significant improvement (p= 0.002) over time with a moderate effect size (d=0.54) and post hoc analysis revealed that this improvement was reached after 6 months compared to baseline (p= 0.009). The intervention group showed no statistically significant improvement over time.

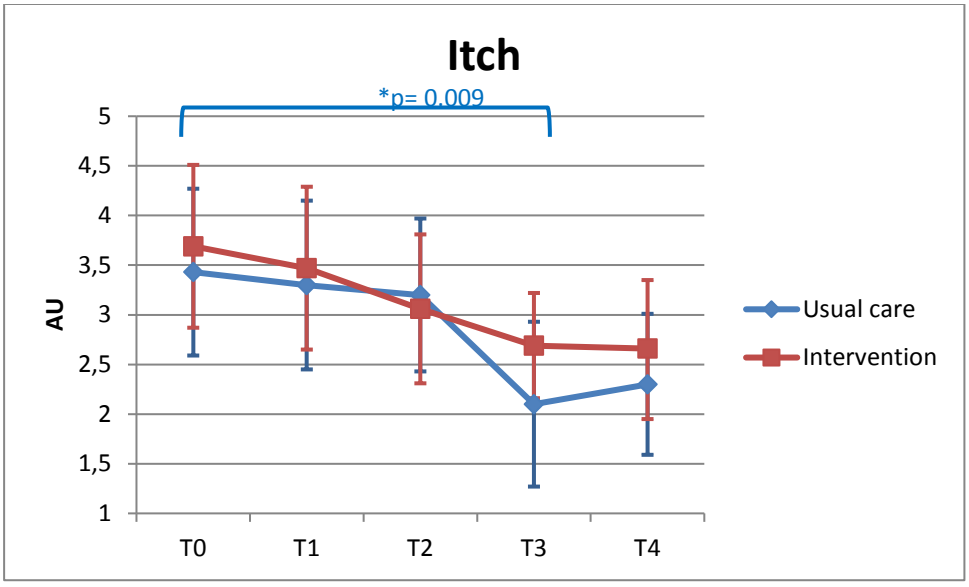

Figure 5-4 Line chart of the itch scores (with confidence interval) in the control group and the intervention group at the different time points.

*The statistically significant improvement over time is illustrated with *.*

5.3.4 The change in touch pressure threshold

In the between group analysis no statistically significant interaction between the intervention and time on TPT could be detected. This was confirmed for the different post-baseline values after corrections for scar age and baseline value.

For the total population the main effect of time showed a statistically significant difference at the different time points (p< 0.0005). Post hoc analysis showed that the significant difference was already reached after 1 month compared to baseline (p< 0.0005).

After within group analysis the usual care group showed no statistically significant improvement (with a small effect size d= 0.2) while the intervention group did reveal a statistically significant decrease of TPT over time (p< 0.005) with a large effect size (d=0.78). Post hoc analysis revealed that this decrease was already reached after 1 month compared to baseline (p < 0.005).

After correction for baseline value and scar age, there was evidence for lower mean values in the intervention group, significantly after 3 months (0.046) and after 1 year (p=0.035) (view Figure 5-5).

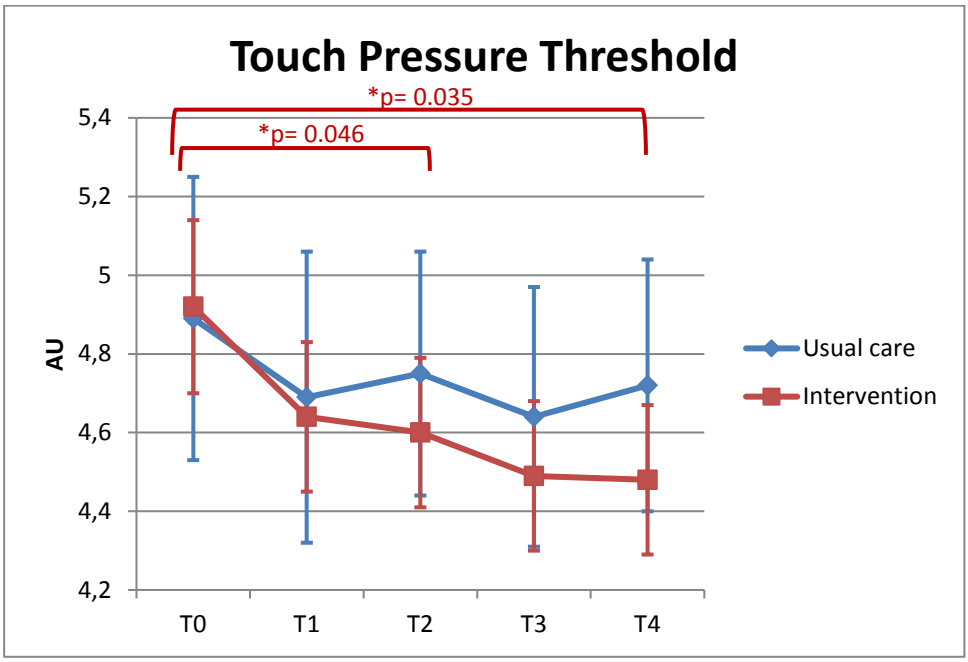

*Figure 5-5 Line chart of the touch pressure threshold scores (with confidence interval) in the control group and the intervention group at the different time points. These results are after correction for scar age and baseline values. The statistically significant improvement over time is illustrated with *.*

5.4 Discussion

The present study was designed to determine the effect of vacuum massage on pain, itch and TPT. The results of this study did not detect evidence that vacuum massage is the preferred additional treatment to improve pain or itch. The between group analyses revealed that there were no statistically significant differences between the groups over time. The intervention group showed statistically significant improvement over time for pain after corrections for baseline value and scar age but showed no improvement over time for itch. However the most obvious finding to emerge from the analysis in the intervention group is the statistically significant improvement for TPT with statistically significant lower mean values for the intervention group at 3 months and 1 year. The usual care group (receiving standard of care) showed statistical significant improvement for pain (after 1 year-compared to baseline) and itch (starting at 6 months) but no significant changes for TPT. From the results of this study only the improvement in TPT can be considered as an added value of the vacuum massage intervention, however not dependent on time.

This study is one of the first to use a mechanical suction device with a clear treatment protocol in the massage therapy of burn scars. The protocol was somewhat consistent with former

clinical trials on vacuum massage. Bourgeois et al. performed LPG treatment (in the treatment for radiation induced skin fibrosis) during 10 minutes, 3 times/week during 1 months. However no suction power, pulsation frequency or specifics on the treatment protocol were described[6]. In the study by Worret et al. (treatment for morphea) only 1 treatment/week was described with very few information on treatment protocol[4].

In previous research on manual massage therapy there is much variability and inconsistency with regard to the treatment protocol and duration of the massage. In the study by Roh et al. Skin Rehabilitation Massage procedure was performed with light stroking of the palm and acupressure on uninjured skin of the forearm and hands, the application of an occlusive dressing, sunscreen and talcum powder. This technique was applied for 30 minutes once a week for 3 months[11]. Cho et al. performed burn rehabilitation massage for 30 minutes 3 times a week (on average 12 treatments during 34 days) with effleurage friction and petrissage after application of a cream, oil and a lotion[10]. Field et al. performed moderate pressure effleurages, pinching and skin rolling with cacao butter during 30 minutes 2 times a week and during 5 weeks. The improvement for pain in this study seemed to be consistent with Cho et al. and Field et al. which likewise found significant improvements for pain[10,12]. This is in contrast with earlier findings for itch in a massage therapy group[10–12] and only clinical improvement were found in a control group[10]. However it is to be noted that in these studies the control groups differed and received no treatment[11] or standard of care similar to our usual care (control) group[10,12]. The standard of care described in this study with the inclusion of hydration, pressure garment and silicone has been reported efficacious in the reduction of pain and itch by several authors[1,27,28]. This may therefore be a plausible explanation for the limited results in our present study for pain and itch. A RCT compared 4 groups (pressure vs silicone vs combined therapy vs control) who all received 15 minutes of massage therapy a day. In all groups an improvement of pain and a decrease in itching was shown[29]. In another RCT the application of a topical silicone gel vs placebo was investigated in which significantly less itching in the silicone group was seen the first 6 months of application[28] and also the use of moisturisers alone could have positive effects on itching[1].Thus pain and itch are already positively affected by pressure and or silicone therapy which are comprised in our usual care.

There are limitations to this study and some methodological consideration must be taken into account. The recruitment of patients was not straightforward and a possible bias may be the allocation method of the patients. Those who were not willing or able to come regularly to the aftercare centre for their treatments and assessments were allocated in the usual care group. This could result in a lower adherence of the usual care group compared to the intervention group.

Besides the allocation by practicality, the standard of care might differ between the 2 groups; in the usual care group treatments were given in a private practice close to home. As already mentioned there was no control group without any kind of massage therapy. After studying the loss-to-follow-up, we noticed a big difference between the usual care group and the intervention group. The reasons for this large loss-to-follow-up in the usual care group are not known and make the study susceptible to selective loss-to-follow-up. A plausible hypothesis could be that the usual care group mostly consisted of subjects not willing or able to come to the aftercare centre. Because of this, we opted for a per-protocol analysis rather than an intention-to-treat analysis. Only those who completed all 5 evaluations were analysed so the remaining 30 patients in the usual care group may be the most motivated patients and therefore explain the findings in the results.

Because of the nature of this study it was not possible to blind the participants or the therapists to the allocation which may also cause important bias on the results. To prevent treatment bias all three observers involved in this study were trained thoroughly in performing the intervention protocols and the inter-observer reliability was already reported to be good for the POSAS and the SWMT[16,30]. The development of hypertrophic scarring is dependent on many different factors. Skin colour, female gender, age, scar location and burn severity are patient related characteristics that have influence on scar formation[31,32]. Mechanical tension, inflammation and wound healing time (for wound closure) are important environmental factors that influence scar formation[33,34]. Although several demographic and clinical patient characteristics were taken into account in this study and no statistical significant changes could be found between the groups (at baseline), the time to wound closure was not assessed. After burns the time to wound healing -which is strongly correlated to the size and depth of the wound- seems the most important prognostic factor for hypertrophic scarring[35,36]. There is growing recognition that statistical significance could be misleading when evaluating treatments, since it may differ from clinical significance[37]. An alternative for statistical significance may be the Minimal Clinically Important Difference (MCID). MCID is the cut off value defined as the smallest difference in scores that is assumed by the patient to be important. However in the burn population there are no cut-off values determined for change in POSAS Pain, POSAS itch or for TPT changes yet. In this study rather low mean values for pain and itch were found at baseline and it is not possible to state whether the change in pain and itch are clinically relevant enough.

Several questions remain unanswered. Despite the statistical improvement for pain and TPT in the vacuum massage group no between group differences were found. The standard of care already may have effects on pain and itch. But from this study no separate effects of hydration, pressure garment and silicone can be drawn. Further work is required to establish the effects of vacuum massage and manual skin techniques. Since no consensus can be found on therapy

frequency nor on duration of treatment, future studies should focus on guidelines for scar management on with well-designed study protocol with large sample size and taking into account cut off values for pain and itch and a combination of subjective and objective assessments to evaluate the effects.

In conclusion these findings show that when treating burn scars with diminished sensation vacuum massage may be a valuable additive.

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6 SHORT-TERM EFFECTS OF VACUUM MASSAGE ON EPIDERMAL AND DERMAL THICKNESS AND DENSITY IN BURN SCARS: AN EXPERIMENTAL STUDY

Published as:

Meirte J, Moortgat P, Anthonissen M, Maertens K, Lafaire C, De Cuyper L, Hubens G, Van Daele U. Short-term effects of vacuum massage on epidermal and dermal thickness and density in burn scars, an experimental study. Burns and Trauma 2016;4:27. doi: 10.1186/s41038-016-0052-x.

Abstract

Vacuum massage is a non-invasive mechanical massage technique invented to treat burns and scars. To date, no effects of vacuum massage on thickness and density of human scar tissue have been reported. The process in which external stimuli are converted into biochemical responses in the cell is known as mechanotransduction. In the skin endothelial cells, fibroblasts and myofibroblasts embedded in the Extracellular matrix (ECM) sense mechanical stimuli (created by vacuum massage) and may promote intracellular processes leading to matrix remodelling. Since mechanotransduction could be a plausible working mechanism for vacuum massage as an anti-scarring therapy this study aims to investigate the short-term effects of vacuum massage on thickness and density of epidermis and dermis in burn scars in order to find prove of ECM remodelling.

A one group experimental study was performed. Patients with burn scars on upper extremities, lower extremities and trunk were recruited for participation in this study. The DUB®cutis 22MHz Ultrasound Scanner was used to assess thickness and density of the epidermal and dermal skin layers. After baseline measurements, vacuum massage was performed according to a pre-defined protocol. Measurements were carried out at 5 min, 30 min, 1 h and 2 h post-intervention.

Thirteen scar sites from 9 different patients were investigated. In 8 out of the 13 scar sites, a disruption of the epidermis was noticed after the vacuum massage. Five minutes after the intervention epidermal density decreased statistically significantly (p= .022) and dermal thickness increased (p=.018). Both changes lasted for more than 1 h, but after 2 h the changes were no longer statistically significant. Dermal density decreased statistically significantly (p=.048) immediately after the intervention and this decrease was still present after 2 h (p=.011).

Preliminary results show that the disruption of the epidermis may indicate that vacuum massage could be able to actually breach the skin barrier. The statistically significant changes in the dermal layers could suggest an increased ECM production after vacuum massage.

6.1 INTRODUCTION

In the burn population hypertrophic scarring occurs in 67% of the cases[1] and often leads to long term impairment and disability[2]. Hypertrophic scars contain an overload of primarily type III collagen oriented parallel to the epidermal surface with multiple nodules containing myofibroblasts, large extracellular collagen filaments and abundant acidic mucopolysaccharides[3]. An overproduction of fibronectin and other fibroblast proteins is demonstrated suggesting either pathological persistence of wound healing signals or a failure to downregulate wound-healing cells[4]. It is generally accepted that hypertrophy and scar contraction can be minimised by reducing mechanical tension[5]. In the skin and other connective tissue, the process in which external mechanical stimuli are converted into biochemical responses inside the cell is known as mechanotransduction[6].

In the skin adherent cells including endothelial cells, fibroblasts and myofibroblasts embedded in the Extra Cellular Matrix (ECM) (or cellular substrate) sense tension (e.g. tension, shear and compression forces) originating from the environment[7]. Tension is transmitted as chemical signals via ECM contacts, leading to reorganisation of the cytoskeleton and the creation of specific signals that modulate gene expression (in the nucleus). Once the cell nucleus receives the appropriate signals, normal cellular processes are engaged. To sum up, the mechanical stimulus on the outside of the cell promotes intracellular processes leading to matrix remodelling[6]. The ECM is the largest component in normal skin, it plays a crucial role in the different wound healing processes[8]. After wound closure (after the inflammation and proliferation phase), the immature scar starts the remodelling phase; the ECM molecules, which are disorganised, are realigned and cross linked. Abnormal ECM reconstruction, particularly abnormal collagen remodelling, during wound healing leads to the formation of hypertrophic scars. In normal scars small parallel bundles of collagen are present with skin appearing flat and discoloured while in hypertrophic scars thin collagen fibres with increased synthesis and crosslinks result in raised scars[9]. The dermal orientation of the fibrous matrix differs from normal tissue[10] and there exists larger collagen density and larger fibre size in scars compared to normal tissue[9]. Hence, the characteristics of scars are a result of altered structure and composition in the dermis and the most important difference with normal skin tissue lies in the orientation of the fibrous matrix[8].

Mechanotherapy or the clinical application of mechanotransduction is the employment of mechanical means for the cure of disease[11]. It has had several definitions and involves the physical therapy (therapeutic exercise, massage therapy and orthopaedic rehabilitation) prescribed to promote the repair and remodelling of injured tissue. It is suggested that physical therapy also helps in healing or homeostasis of tissue outside the musculoskeletal system and may be able to oppose against specific pathophysiology and diseases[11]. Recently new insights in the working mechanism of

physical therapy have emerged and have led to a new definition for mechanotherapy: therapeutic interventions that reduce and reverse injury to damaged tissue or promote the homeostasis of healthy tissue by mechanical means at the molecular, cellular or tissue level[11].

Physical therapy modalities for scar treatments involve amongst others massage therapy as best practice[12], which can be manual or mechanical. One of these mechanical massage techniques is vacuum massage, also known as depressomassage[13], vacuotherapy[14] or Endermology[15®]. Vacuum massage lifts the skin by means of suction, creates a skin fold and mobilises that skin fold[15–17]. In the late 1970's this therapy was introduced to treat traumatic or burn scars[18]. Although vacuum massage was invented to treat burns and scars, one can find very few literature on the effects of this intervention. The effectiveness of vacuum massage has however not been widely proven. This study is part of a larger study in which the clinical effectiveness of vacuum massage is examined (a manuscript on the long-term effects of vacuum massage on clinical parameters is in preparation for submission). However we found the underlying mechanisms of vacuum massage and mechanotherapy very important to give insight into what occurs in the scarred skin after mechanical massage. Massage therapy influences dysfunctioning of a burn patient in several domains of the International Classification of Functioning, Disability and Health (ICF). The ICF was created by the World Health Organisation and is a framework that describes the impact of a condition and incorporates physical, emotional, environmental and social aspects of daily functioning[19]. The domains of the ICF describes impairments in body structures and body functioning, activity limitations and participation restrictions. Effects of massage therapy on impairments in body functions (e.g. on pain and itch[20–22]) have been demonstrated in the burn population but we found it important to know what influence is seen on body structures (actual change in the human skin).

Since mechanotransduction due to mechanical forces such as shear tension or compression could lead to collagen alterations and collagen re-orientation this could be a plausible working mechanism for vacuum massage as an anti-scarring therapy. Significant changes in dermal thickness and density assessed by ultrasonography may be related to oedema and increased ECM production[23]. Results on animal models showed that as a result of vacuum massage collagen content increased to as high as 130% in long term treatments[16]. Effects were found on collagen alteration of fibroblasts phenotype and collagen orientation (more longitudinal). Results were dependent on the operator using the device and the results were proportional to the number of treatments.

The goal of this study was to assess changes in the scar at a structural level (ICF domain body structures) in a non-invasive way. Thickness together with height and depth of the scars can be measured with ultrasonography[24]. The change in scar thickness measured with ultrasound has been used to assess the maturation of hypertrophic scars[25,26] and can be used to compare hypertrophic

scar thickness between patients[26] and evaluate intervention outcomes[25]. Ultrasonography can be used to examine therapeutic strategies on healing scars[27]. In dermatology high resolution B-scan ultrasound has enabled non-invasive assessment of different skin pathologies and has provided morphologic information of skin structures[28].

This study seeks to prove the earlier suggested effects and the remodelling of the ECM[6] by evaluating the short term effects of vacuum massage on epidermal and dermal thickness and density in scarred skin measured with a high resolution B-scan ultrasound.

6.2 METHODS

6.2.1 Ultrasound measurement

With ultrasonography, high frequency sound pulses are beamed into the skin and reflected at structural interfaces within tissues, where high acoustic impedance gradients are encountered[28]. For this study, thickness of the scars was determined by high frequency ultrasound 22MHz (DUB®Cutis, Taberna pro medicum, Lueneburg, Germany) and expressed in micrometres (µm). Using this 22MHz transducer it was possible to visualise structures up to approximately 8 mm in depth. Sound is coupled from the transducer to the tissue by water in the scanning head of the probe to provide minimal attenuation of the ultrasound signal[29].

The probe was placed perpendicularly on the skin and a live feed displayed an area capable of measurement. Once completed, a snapshot of the ultrasound output was saved in the software on a computer. The A-scan image revealed the amplitude of the signals reflected by the borders of the different skin layers. The thickness of the dermis was measured by identifying the epidermis-dermis and dermis-subcutis interfaces[30] and was calculated by dividing the velocity of the ultrasound signal in the skin (approx. 1600 ms^{-1}) by the transmission time of the signal[31]. The two-dimensional B-scan was used to calculate densitometric values (or density) of each lesion using pixel density converted into a 256-colour scale[32]. The region of interest was determined and the values for epidermal and dermal thickness and density were registered. The ultrasound examination of the scars demonstrates the architecture of the skin. There is an entry echo line representing the gel-water-stratum corneum echo signals from the epidermis, the next change in echogenicity is the interface with the dermis and the start of the deep echo-lucent (black) area is the interface between dermis and subcutaneous fat[33]. The region of interest for which the values were to be determined were delineated by hand. The test site was marked with a surgical pencil, drawing the boundaries of the probe head (placed perpendicularly to the skin) and taking a picture to assure body position and

exact location of the probe for the repeated measurements. The assessor in this study was a physical therapist trained in ultrasound probe application. The treatment was always performed by the same physical therapist specialised in vacuum massage therapy.

6.2.2 Participants

Patients were recruited in Oscare, organisation for burns, scar aftercare and research in Antwerp, Belgium. Only patients with an age between 18 and 70 years qualified for the present study. Patients with Caucasian skin type and burn scars located on upper extremities, lower extremities and trunk (excluding the sole of the feet and hand palms) were included because of accessibility of the measure probe. Women in their last three months of pregnancy, patients with extremely high sensitivity for skin irritations, central neurological conditions, peripheral paralysis and diabetes were excluded for selection. Furthermore patients who were obliged to take one of the following medications: Aspirin, Warfarin, Marcumar, Methrotrexate, Cyclosporin were excluded.

6.2.3 Assessment and Intervention Protocol

Informed written consent was obtained from all patients. The assessment in this study started with a single observer scanning a marked (exact location of the probe and photographed) area of the scarred skin with the DUB®Cutis ultrasound followed by a single treatment with the PRUS device (F care systems NV, Antwerp, Belgium), subsequently followed by repeated ultrasound scanning at different timepoints. The application with the PRUS vacuum massage, which is shown in Figure 5-1, was performed for 10 minutes covering an area of 10 cm^2 (the exact protocols are presented in Figure 6-1). The study protocol was approved by the ethics committee of the Hospital Network Antwerp (ZNA), Belgium (Ethical committee 009OG031, study number EC4549).

Measurement Time	Description	Measurement
T0	Baseline measurement Observer before application	Dubcutis® US scan
Treatment	Vacuum massage application 10 min	**PRUS Device**
T1	5 min after application	Dubcutis® US scan
T2	30min after application	Dubcutis® US scan
T3	1h after application	Dubcutis® US scan
T4	2h after application	Dubcutis® US Scan

	Value	Comment
Suction Power	250 mb – 900 mb	Depends on location
Duration	10 min	An area of $10cm^2$
Pulsation	0,25 – 0,50 Hz	6″ W – 2″ R

Figure 6-1 Assessment protocol with inclusion of the treatment protocol of the vacuum massage

US= Ultrasound, mb= millibar, Hz= hertz, W= working time, R= resting time, "= seconds

6.2.4 Statistics

All data was analysed using SPSS 20 software package for Windows. The normality was analysed using the Kolmogorov Smirnov test. The data followed normal distribution; hence, parametric tests were performed. Descriptive statistics were generated and paired sample t-tests with estimates of effect size were calculated to determine whether there was a statistically significant mean change in the epidermal and dermal thickness and density between the time points. We calculated effects size as Cohen d, with d defined as the difference between the 2 means divided by the pooled SD for those means. A d value of 0.20 is described as small, 0.50 as moderate and 0.80 as large[34]. Significance was set at 0.05. The bar charts in figures 6-3 to 6-5 display the mean and the standard deviations.

6.3 RESULTS

This preliminary study consisted of 13 post-burn scar sites from nine different patients, three women and six men. The mean age was 24.56 years ± 13.26, mean scar age was 16.26 months ± 14.27 and scars were located on the upper extremities (n=3) and lower extremities (n=7) and on the trunk (n=3). As presented in Figure 6-2, we found a disruption (visual presence of multiple echo lucent areas) of the epidermis in 8 out of 13 scar sites after the vacuum massage.

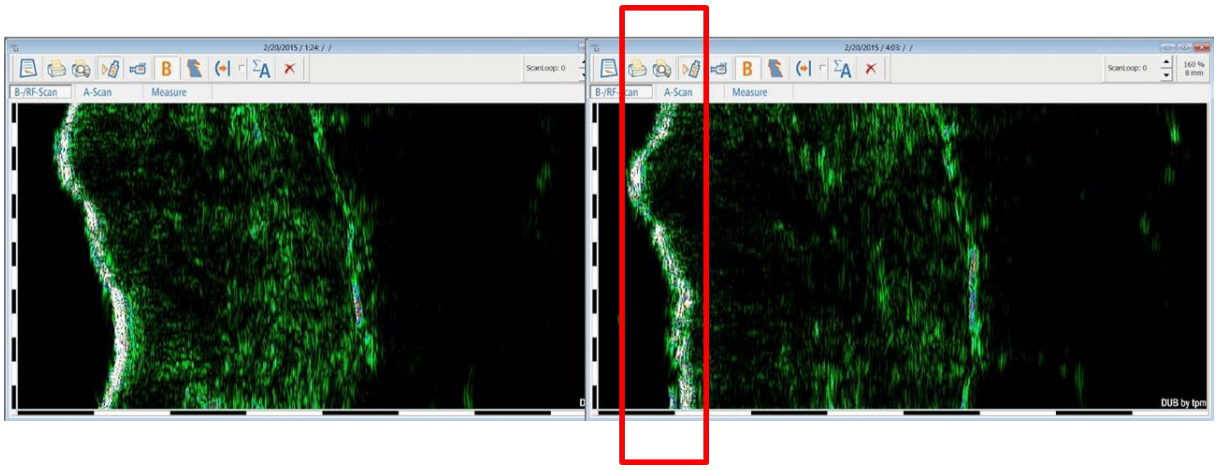

Figure 6-2 Illustration of disruption of the epidermis visible on the DUB®Cutis dermascan B image

No significant changes were found in the epidermal thickness. Immediately after the intervention (T1) the epidermal density decreased statistically significant (p= 0.022) with a moderate effect size of -0.73. Two hours after the intervention (T4) the epidermal density did not show any significant changes (p= 0.096) compared to baseline and the effect size decreased to -0.61. This is illustrated in Figure 6-3.

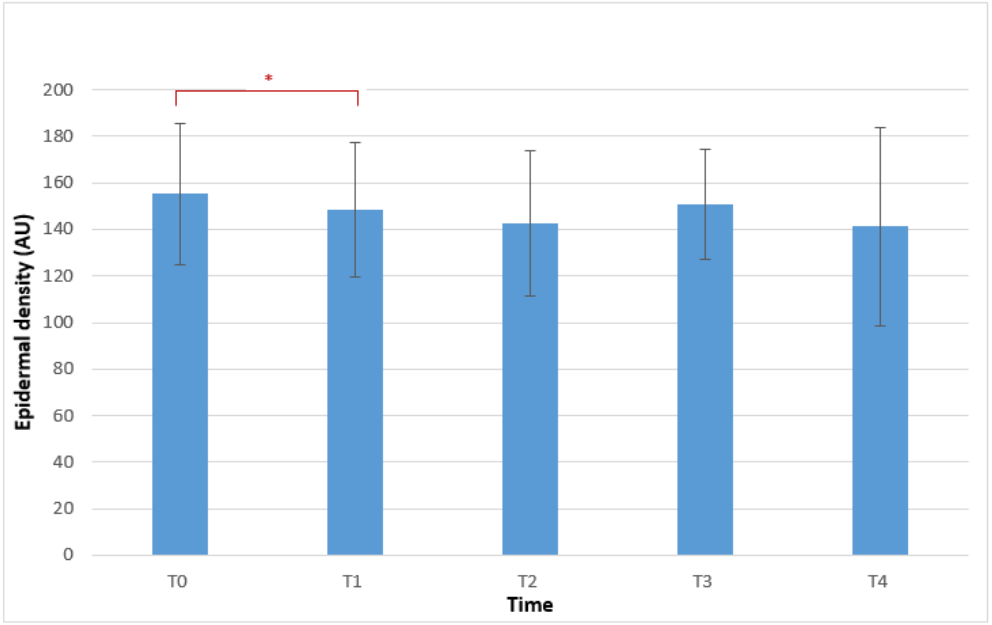

Figure 6-3 Bar chart showing the data distribution summaries of the epidermal density at the different timepoints.

**= p < 0.05. Bar chart showing the mean and the error bar represents the standard deviations. T0= baseline measurement, T1= 5 min after application, T2= 30 min after application, T3= 1h after application, T4= 2h after application, AU= arbitrary units*

Immediately after the intervention, the dermal thickness increased statistically significant (p= 0.018) with a moderate to large effect size of 0.76. After half an hour, the thickness decreased compared to the previous measurement but was still statistically significant increased

when compared to the baseline measurement (p= 0.046) . After one hour, we still observed a significant increase compared to the baseline measurement (p= 0.013). Although a decrease was observed two hours after the intervention the dermal thickness did not show any significant changes (p= 0.06) compared to baseline and the effect size decreased to 0.57 (Figure 6.4).

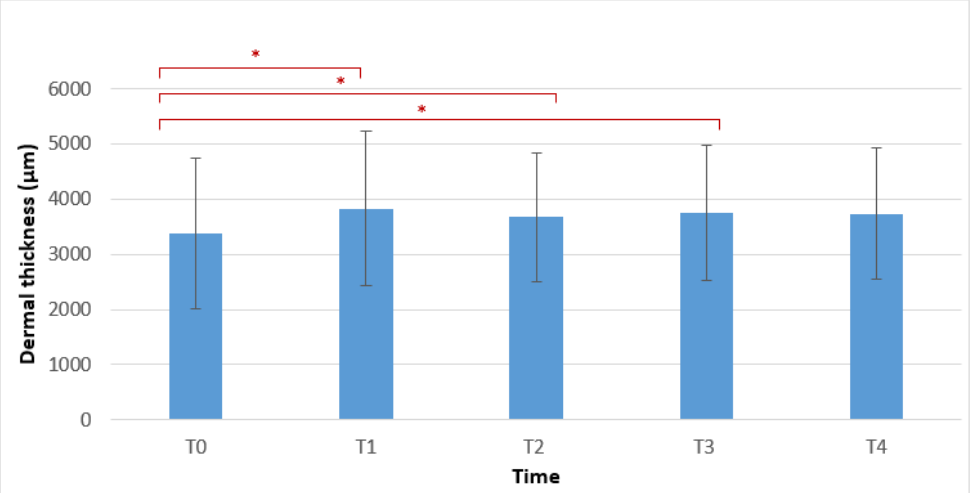

Figure 6-4 Bar chart showing the data distribution summaries of the dermal thickness at the different timepoints.

**= p < 0.05. Bar chart showing the mean and the error bar represents the standard deviations. T0= baseline measurement, T1= 5 min after application, T2= 30 min after application, T3= 1h after application, T4= 2h after application, µm= micrometre*

Immediately after the intervention the dermal density decreased statistically significant (p= 0.048) with a moderate effect size of -0.61. Two hours after the intervention the dermal density was still decreased statistically significant (p= 0.011) with a large effect size of -0.83 (Figure 6-5).

The echo images prior to treatments revealed nodular arrangement in the dermis. As illustrated in Figure 6-6, a more longitudinal arrangement was observed after vacuum massage treatment.

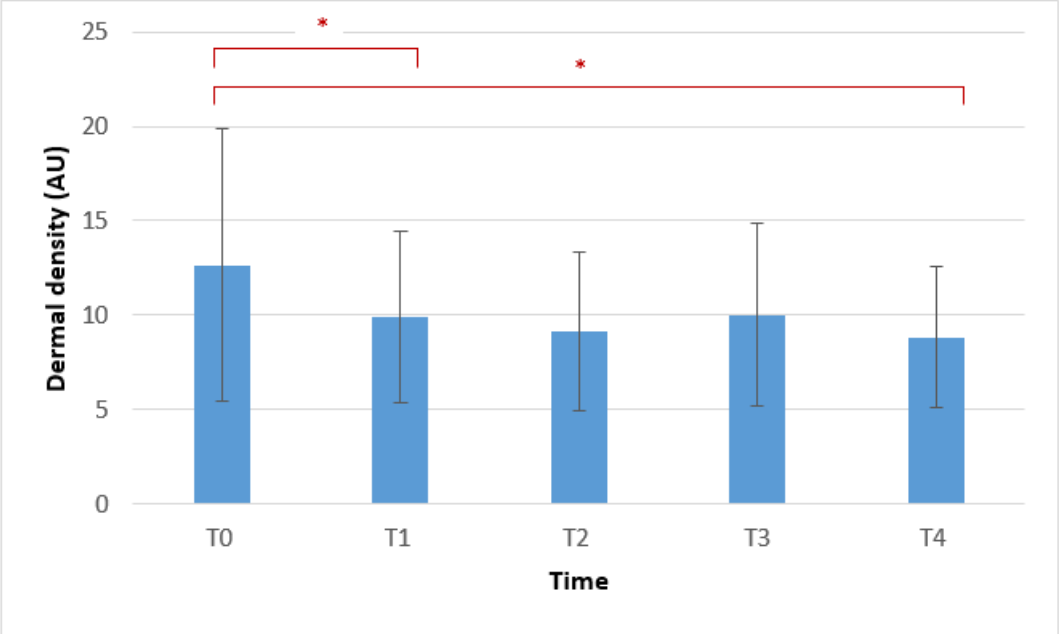

Figure 6-5 Bar chart showing the data distribution summaries of the dermal density at the different timepoints.

**= p < 0.05. Bar chart showing the mean and the error bar represents the standard deviations. T0= baseline measurement, T1= 5 min after application, T2= 30 min after application, T3= 1h after application, T4= 2h after application, AU= arbitrary units*

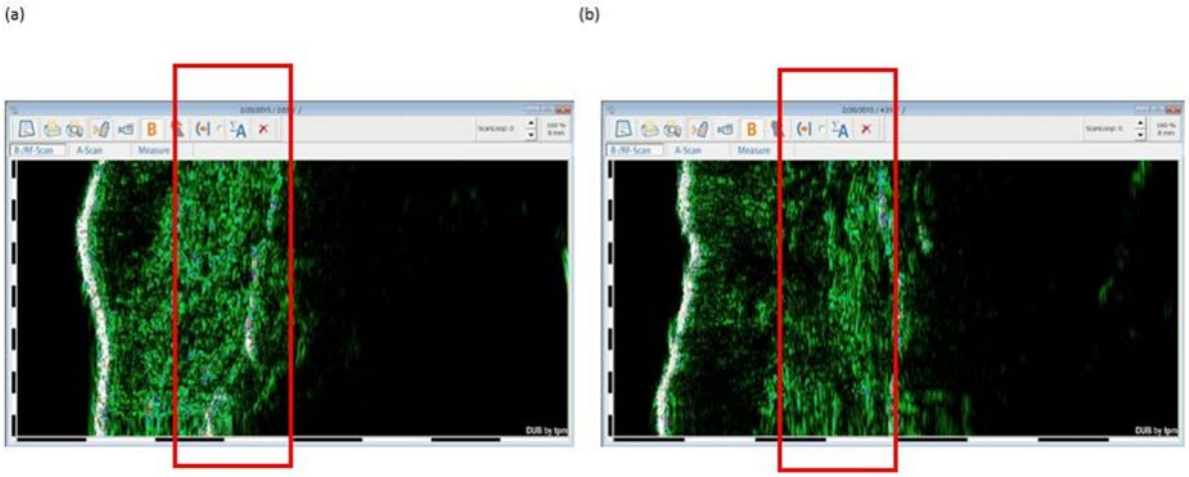

Figure 6-6 Illustration of the dermal arrangement visible on the DUB®Cutis dermascan B image

(a) prior to treatment with more nodular arrangement; (b) post treatment with more longitudinal arrangement

6.4 DISCUSSION

This study investigated the short term effects of vacuum massage on physical scar properties and found statistically significant changes in the epidermal density immediately after the intervention. Dermal thickness increased significantly immediately after the intervention; after 1 hour the dermal thickness decreased significantly compared to baseline and a trend was seen at 2 hours compared to baseline. Dermal density decreased significantly after the vacuum massage treatment and even at 2 hours post-treatment, this decrease was still significant compared to baseline.

Interpretation of the findings

These findings are in line with the findings of Hesselstrand et al. (2008) who also found an increase in dermal thickness and reduced echogenicity in patients with Scleroderma which was explained by oedema formation and an increased ECM production[23]. The disruption of the epidermis (assessed by the visual presence of multiple echo lucent areas) and the decrease of the epidermal density might indicate that the intervention could be able to actually breach the skin barrier[17].

The initial pre-intervention echo images revealed a nodular arrangement in the dermis; after the intervention, the dermal fibre arrangement was more longitudinal and wave like patterned. This may indicate collagen realignment due to the vacuum massage. For dermal density the effects even last until two hours after the intervention, which could indicate that ECM restructuring still goes on. These results are in line with the findings of Adcock et al. who reported a reorganisation of the ECM with increasing collagen synthesis and realignment of the collagen fibres after vacuum massage on Yorkshire pigs[17], both signs of ECM restructuring. We hypothesised that vacuum massage may be a potential anti-scarring therapy leading to collagen re-orientation drawn on the underlying concept of mechanotransduction. The observed collagen arrangement in the current study needs further data research with histological examination to establish these dermal changes, and further exploration of mechanotransduction pathways in vacuum massage is needed. Somewhat similar to our findings a recent study on the effect of pressure therapy in post burn hypertrophic scars revealed reduced dermal cell density and altered collagen fibre arrangement in histological examination[35]. Myofibroblasts responsible for pathological scar formation in hypertrophic scars were abundantly present in the pre-treated scars; the applied mechanical pressure therapy significantly suppressed myofibroblast activity after which the myofibroblasts disappeared by apoptosis leading to improved collagen fibre alignment[35]. Another recent study reviewed the role of mechanical forces at the molecular and tissue level in various physical therapy treatments (e.g. massage and shockwave therapy)[11]. The researchers emphasised the beneficiary role of vacuum-assisted closure (VAC) or

negative pressure wound therapy (NPWT) as a 'mechanotherapy'. Since their mechanism is similar to that of vacuum massage a similar beneficiary role may be expected.

Efficacy of massage has been described in prior research to stimulate cell signalling pathways and activate potentially immunomodulatory pathways[36]. Massage reduces cellular infiltration, inflammation and oedema in muscles[37]. This study although preliminary shows positive effects of mechanical massage on the physical properties of scarred skin. Mechanotherapy together with mechanotransduction is a promising field that may promote healing of tendon, muscle cartilage bone[6] and also scarred skin[11]. Only the tip of the iceberg has been unravelled and there is abundant room for further research in determining the exact effects of massage and vacuum massage on post-burn skin physical structures.

Methodological considerations

There are several weaknesses in this study that should be addressed in future studies. Scar sites were located on the upper, lower extremities and the trunk in this study and literature on normal skin has shown that there are substantial differences between skin thickness of the upper extremity and the lower extremity[38]. To reach a statistical power of at least .80, the required sample size for this investigation should be at least 17 patients. The average age of the scars was rather high and had a large SD; therefore the results of this investigation cannot be generalised. The echogenicity of the skin depends on the dermal water content, on the amount of collagen and on the skin configuration[28]. The echo poor images recorded after the vacuum massage treatment may indicate a change of the collagen structure but can also be the result of an increase in water-binding properties or increased dermal water content[28]. Various high frequency ultrasound instruments exist to evaluate scar thickness varying in costs, size and applicability. Although other authors demonstrated good inter- and intra-reliability for high-frequency ultrasound testing in post-burn scars[27] only recently the DUB®Cutis ultrasound scanner was found reliable for dermal thickness and density for repeated measures by one or two different observers[39] in post-burn scars. Moreover, the instrument was found reliable to assess epidermal thickness for repeated measures by one observer. Comparing echo images with histological examination and this within a RCT design would be the next step to establish the current epidermal and dermal findings as a result of vacuum massage treatment. The short term effects of vacuum massage were chosen to minimise BIAS by other treatments (pressure garments, hydration, silicone, physiotherapy). In this short time period the patients remained in the centre (in the same room and if possible in the same position), this facilitated relocations.

Some authors describe ultrasonography as complicated and requiring professional training[40], we agree that the probe application acquires thorough training since pressure influences the results of the epidermal layer. Relocation of the measurement site must be done under strictly

standardised conditions. Moreover we recommend to interpret a series of scans from the same patients together to enhance exact relocation of the measurement site. Despite the limitations this study has some strengths. This study is the first to describe and hypothesise mechanotransduction as a possible working mechanism of vacuum massage on post-burn scars.

In conclusion, the disruption of the epidermis might indicate that the effect of vacuum massage could be able to actually breach the skin barrier. The statistically significant changes in the dermal layers suggest oedema formation and an increased ECM production which could be attributed to an immediate mechanotransduction effect of vacuum massage on the remodelling of the ECM. Further research is needed to elucidate the preliminary findings of this study and the effects of different forms of mechanotherapy on the physical scar properties and beyond in patients with post-burn scars.

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GENERAL DISCUSSION

This thesis focused on the dysfunctioning of patients with burn scars and used the **International Classification of Functioning, Disability and Health** (ICF) framework to describe the different assessment tools and questionnaires. The first objective was to explore and optimise the **quality of burn measures**. First, four studies were conducted in order to evaluate the quality of both objective and subjective measures that are being used to evaluate the broad impact and thus dysfunctioning post burn within different domains of the ICF framework. Objective measures that assess impairments in Body Functioning and patient reported outcome measures (PROMS), more specifically health-related quality of life (HRQOL) questionnaires were investigated in depth. Second, the **effects of vacuum massage** on impairment in skin related Body Structures, sensory function pain and pruritus were explored with two physiotherapeutic clinical intervention studies. The discussion will start by summarising the main findings of this dissertation; in addition, it will discuss some methodological considerations and other themes concerning the impact of a burn injury. Some recommendations for future research will be given and finally a general conclusion will be presented.

Research Questions

In Part 1 'Quality of Burn Measures' the following research questions were addressed:

- What is the reliability of the Semmes Weinstein monofilament test within burn scars and healthy controls using the ascending descending procedure?
- What is the intra- and interrater reliability, validity and feasibility of the Scarbase Duo® for use in research and clinical application in burn scars?
- What are the most frequently used HRQOL measures? Are they able to describe the broad spectrum of dysfunctioning and the different domains of the ICF framework? What aspects do they measure and what is left uncovered?
- What is the convergence and discriminant validity between HRQOL measures in burn populations?

In Part 2 of this thesis 'Vacuum Massage' the following research questions were addressed:

- What is the effect of vacuum massage on pain, itch and touch perception threshold in burn scars?
- What are the short-term effects of vacuum massage on epidermal and dermal density and thickness in burn scars?

Summary of the main findings

In **Chapter 1**, we investigated the reliability of the Semmes Weinstein monofilament test (SWMT) to assess touch pressure threshold (TPT) or the sense of touch in burn scars and healthy

controls with the 'ascending descending' measurement procedure. In the scar group intrarater ICC value was excellent (ICC=0.82). Within the control group also excellent intrarater reliability (ICC=0.81) was found. The interrater reliability was excellent in the scar group (ICC= 0.91) and fair to good in the control group (which included age and gender matched controls (ICC= 0.73). The SWMT was demonstrated as feasible and reliable to objectify the touch pressure threshold in upper extremities burn scars and healthy subjects.

Chapter 2 described the reliability and validity of an objective dual scar assessment tool (the Scarbase Duo®) which is compact and easy to use to assess transepidermal water loss (TEWL) with the Tewameter® and colour with the Mexameter® in burn scars. For colour both erythema and melanin components were evaluated. TEWL was measured through an open chamber system and colour was assessed via narrow-band spectrophotometry, producing values for haemoglobin and melanin. Validity was assessed compared to Dermalab® for TEWL and the Minolta Chromameter® for colorimetry measurements. The Scarbase duo® TEWL mode showed excellent reliability when used on scars for both intra- (ICC= 0.95) and interrater (ICC= 0.96) measurements. The erythema component of the colorimetry mode showed good reliability for use on scars for both intra- (ICC= 0.81) and interrater (ICC= 0.83) measurements. Melanin values showed excellent reliability for both intra- (ICC= 0.97) and interrater (ICC= 0.97). The TEWL function had excellent correlation (r= 0.93) with the Dermalab ® proving convergent validity, the colorimetry erythema value had moderate correlation (r= 0.72) with the Minolta Chromameter®. The Scarbase Duo® was shown to be reliable for repeated measures and between two raters for TEWL and colour, two valuable predictors of scar maturation. We recommend the use of this valid, small, affordable light-weight testing device with immediate data logging on the computer for the evaluation of treatment effects on burn scars. Standardised measurement conditions are recommended taking into account even pressure application for the colour probe to avoid blanching, and limitations of air currents for the open-chamber TEWL probe.

In the **third chapter** the most commonly used HRQOL measures were sought. Two generic measures, the Short Form-36 items (SF-36) and the European Quality of Life 5 Dimensions (EQ-5D), and the Burn Specific Health Scale Brief (BSHS-B) were by the content of their subscales classified within the ICF framework. Overlaps and gaps were explored and revealed that the BSHS-B covered most domains, had 5 unique subscales (Heat sensitivity, Sexuality, Hand function, Body image and Treatment regimens) and was the only tool to include Personal Factors. The SF-36 had one unique subscale (Vitality), only one subscale within the Activity domain and similar to the EQ-5D no Contextual Factors were addressed by this questionnaire.

The convergent validity of the EQ-5D, the SF-36 and the BSHS-B was empirically evaluated in **Chapter 4** in a prospective multicentre study and supported the prior theoretical overlap. The psychometric assessment of the relationship between the EQ-5D, the SF-36 and the BSHS-B shows that convergence is higher between the generic measures (EQ-5D and SF-36) as compared to the BSHS-B. Both generic scales performed well regarding discriminant validity. Additionally, the ICF framework previously appeared useful to identify gaps regarding domains that are currently overlooked. Consequently, there is room for improvement, particularly regarding the burn-specific measure. This study illustrated that a short generic scale can provide interesting information but should be combined with a more comprehensive condition-specific scale in order to capture the full impact. Overall, this study supports the view that currently the most frequently used scales to measure functioning fall short to measure the full impact of a burn injury.

In **Chapter 5** the effects of vacuum massage on pain itch and sensory perception was explored in a comparative study between a usual care group who received standard of care and an intervention group who received vacuum massage in addition. Between-group analyses revealed no statistically significant differences between the intervention group and the usual care group over time. Within-group analysis for pain revealed for both groups a statistically significant improvement over time after corrections for scar age and baseline value -analysis with transformed data- both groups (control p= 0.003, intervention p= 0.017). In the within-group analysis for itch the usual care group showed a statistically significant improvement (p= 0.002) over time which was reached after 6 months compared to baseline (p= 0.009). The intervention group showed no statistically significant improvement over time. Evidence was found for lower TPT values in the intervention group after correction for baseline value and scar age. Significant differences were measured after 3 months (p= 0.046) and after 1 year (p=0.035). In conclusion, the effects show that -when treating burn scars with diminished sensation- vacuum massage may be a valuable additive.

The short-term effects of vacuum massage on epidermal and dermal Body Structures were presented in **Chapter 6**. Moreover the possible role of vacuum massage as a form of mechanotherapy was described, explaining the possible working mechanism for vacuum massage as an anti-scarring agent. Significant changes (p= 0.022) in the epidermal density were found immediately after the vacuum massage. Dermal density decreased significantly after application (p= 0.048) and was still present after two hours (p= 0.011). A disruption of the epidermis in the majority of the cases and the significant decrease in density indicated that the intervention might actually breach the skin barrier and could lead to extracellular matrix remodelling after the treatment

General discussion

In this final discussion we explore several themes in-depth concerning the consequences of the obtained results reflecting on the applicability of our findings beyond burn patients, along with clinical implications for researchers and clinicians and future research directions for mechanotherapy. The discussions that emerge from this dissertation are: (a) the ICF as a framework in (burn) scar rehabilitation, (b) objective evaluation of hypertrophic scars in general, (c) mechanotherapy a new era in physical therapy, (d) practical/clinical implications and (e) future research recommendations.

The ICF as a framework in (burn) scar rehabilitation

As already elaborated in the introduction of this thesis, the ICF is a framework to describe the (dys)functioning within a health condition or disease and is frequently used to describe a single patient's dysfunctioning in order to set up therapy goals. It can also be used to compare or simply classify the content of questionnaires. It is believed that functional status information of patients will soon be required in managed-healthcare contexts because functional status information may be a better predictor of health-system usage than the obvious diagnostic procedures and labels[1]. Clinicians are using PROMS more and more to guide and audit routine care. Within clinical practice they can assist physical therapists in their clinical reasoning process and in both patient's evaluation and treatment with focus on the patient's perspective[2].

HRQOL are PROMS that address symptoms as well as physical status, psychological status and social functioning from the patient's perspective[3] are very important in patients with post burn scars. Ideally generic and disease-specific measures should have minimum overlap[4]; this is not the case in the frequently used HRQOL measures in the burn patients population. No linking rules[5], to link health status measures to the ICF, were applied in the classification study in Chapter 3 and no degrees of agreement were performed between the researchers who performed the ICF linkage procedure.

In the prospective multicentre study of Chapter 4 the convergent and discriminant validity of the BSHS-B, the SF-36 and the EQ-5D was investigated, however no change over time was assessed. Assessing responsiveness in HRQOL requires instruments capable of capturing even small changes that are important to patients[6]. In a literature review the relative responsiveness of generic and specific quality of life instruments was assessed in 43 randomized controlled trials that compared generic and specific instruments. This study concluded that specific measures are more

responsive[6]. In burn literature studies on the responsiveness of HRQOL measures are scarce. In contrast to the overall assumed greater responsiveness in specific measures the generic SF-36 showed greater responsiveness than the specific BSHS-B in burn survivors [7]. As the BSHS-B performed less well in both discriminant validity and responsiveness, there seems room for improvement and modification[8].

Both the investigated PROMS and objective measures from this thesis were classified within an ICF form (Figure 7-1). In this form aspects that (for the patient and/or the therapist) require attention (e.g., severe problems with mobility, >3 for POSAS pain) can be written down. This thesis repeatedly demonstrated the benefit of the ICF model within the physical therapy management (both assessments and therapy) of patients with hypertrophic scars. Throughout this thesis items of the POSAS (namely pain and itch) and commonly used HRQOL measures were elaborated on, however the link between the two was not explored. The ICF model (Figure 0-1) explicitly acknowledges bidirectional relationships among domains of function meaning there are interactions between the different components[9]. This raises another research question that should be considered as recommendation for future research; can scar characteristics -involving impairments in body functioning- be linked or even predict activity limitations and participation restrictions evaluated by HRQOL subscales?

Objective evaluation of hypertrophic scars

Hypertrophic scars after burn injury are characterised by several impairments that affect appearance (red colour, elevated skin) as well as function of the skin (pain sensations, changes in sensitivity and a changed skin barrier function)[10]. Objective tools are necessary to evaluate effectiveness of burn scar treatments[11]. They are more reliable than subjective evaluations and thus recommended to perform accurate evaluations besides subjective scar scales[12]. However, objective measures assess a specific scar feature and not the overall quality of a scar[13]. The objective measures described and investigated in this doctoral thesis are the SWMT and the Scarbase Duo® which assess TPT, colour (by means of vascularity/erythema and pigmentation/melanin) and TEWL respectively. Both studies used the Guidelines for reporting reliability and agreement studies[14] to report the findings.

The TPT assessment tool with the Semmes Weinstein complete kit, consisting of 20 sequentially graded thickness monofilaments, can accurately categorise loss of function and detect first signs of recovery[15]. Our study had a clear measurement protocol and demonstrated the feasibility and reliability of the ascending descending procedure with the SWMT. Mean scar age was

rather high (±83 months) and only upper extremities were tested. Moreover, this study did not take into account injury related factors (e.g., cause of burn, burn depth, surgical intervention). A downside to TPT measurement is that subjects need to be immobilised and focussed for approximately 10 minutes and environmental stimuli may influence testing. Although the SWMT complete kit is useful for detecting first signs of sensation recovery[15] for routine burn scar follow-up outside the research centre this tool seems less applicable due to the cost and bulky size.

Scar erythema and TEWL are two valuable predictors of burn scar maturation[16] and are combined in the Scarbase Duo® device. It is an easy to use light body objective assessment tool with 2 small probes and immediate data logging on the computer. The Scarbase Duo® was found valid and reliable for repeated measures and between 2 observers. The results for the Mexameter establish earlier findings on its reliability[13,17,18]. Our study was the first to test the Tewameter's reliability in scars and resulted in slightly favourable results compared to findings on Dermalab's reliability[19]. The spring-mounted central portion in the Mexameter creates even pressure per measurement and avoids blanching. The open chamber system of the Tewameter is less favourable since turbulence at the test site may be caused. In reliability testing the observers' ability to precisely relocate the previous measured site is also a common source of error[20]. Table 7-1 summarises the clinimetric properties of the objective measures investigated in this thesis.

Table 7-1 Clinimetric properties of the objective measures investigated in this thesis

	Reliability	**Validity**
Mexameter	intraICC$_{scar}$ ≥ 0.81 with SEM ≤ 39.45 intraICC$_{healthy\ skin}$ ≥ 0.94 with SEM ≤ 15.74 interICC$_{scar}$ ≥ 0.83 with SEM ≤ 38.88 interICC$_{healthy\ skin}$ ≥ 0.96 with SEM ≤ 13.36	E-index-Chromameter *a value$_{scar}$ ICC= 0.47 r= 0.72 E-index-Chromameter *a value$_{healthy\ skin}$ ICC= 0.93 r=0.93
Tewameter	intraICC$_{scar}$ = 0.95 with SEM 1.17 intraICC$_{healthy\ skin}$ = 0.87 with SEM 0.74 interICC$_{scar}$ = 0.96 with SEM 1.12 interICC$_{healthy\ skin}$ = 0.90 with SEM 0.75	Mexameter-Dermalab$_{scar}$ ICC= 0.81 r=0.93 Mexameter-Dermalab$_{healthy\ skin}$ ICC= 0.52 r= 0.72
Semmes Weinstein aesthesiometer	intraICC$_{scar}$ = 0.82 with SEM = 0.33 intraICC$_{healthy\ skin}$ = 0.81 with SEM = 0.27 interICC$_{scar}$ = 0.91 with SEM = 0.21 interICC$_{healthy\ skin}$ = 0.73 with SEM= 0.12	Not compared to a gold standard

Mechanotherapy a new era in physical therapy

The physical therapy discussed in this thesis involved the effects of vacuum massage on impairments in Body Functions with the comparative study (Chapter 5) and on impairments in Body Structures with the experimental study (Chapter 6). The effects of vacuum massage on the broader

impact (HRQOL) were not investigated and the role of mechanotransduction within other physical therapy techniques was not explored.

The comparative study on the long-term effects of vacuum massage on pain itch and TPT was one of the first to use a mechanical suction device with a clear intervention protocol as massage therapy for burn scars. Although no statistically significant differences between the groups could be found the effects of vacuum massage were promising for TPT. The standard of care applied in both groups with hydration, pressure therapy and silicone may explain the limited results for pain and itch since these therapies already proved to positively influence those parameters[22,23]. The recruitment was not straightforward in this study and allocation was done by practicality. There was a large heterogeneity in burn patients (e.g., more men in the vacuum massage group than in the control group). No control group without any form of manual massage was present nor was the standard of care in both groups exactly the same. There were small changes in mean pain and itch values, however no clinically important differences could be given since cut-off values for pain, itch and TPT do not exist in burns literature.

The experimental study on the short-term effects of vacuum massage revealed effects of this mechanical massage within skin structures made visible with ultrasound images. After treatment collagen fibres were more longitudinal and wave patterned arranged compared to the pre-test images. Dermal density changed significantly which could indicate ECM restructuring. We hypothesised that vacuum massage is a potential anti-scarring therapy leading to collagen re-orientation drawn on the underlying concept of mechanotransduction. The observed results in this preliminary study need histological examinations to confirm these findings.

In recent years there has been an increasing interest in the mechanobiology of scars. The influence of mechanical forces on skin has been examined since 1861 when Langer first reported the existence of lines of tension in cadaver skin[24]. Internal tension in the dermis leads to cell – extracellular matrix and cell – cell interactions transferring external mechanical forces into biochemical signals inside the cell[25]. Khan et al. introduced the term ‘mechanotherapy’ and presented the current scientific knowledge underpinning how mechanical load may be used therapeutically to stimulate tissue repair and remodelling[26]. Recent developments in mechanobiology illuminated the effects of physical forces on cells and tissues and have led to the realisation that “the old physical therapy model” should be updated. Recent studies showed how mechanotherapies target particular cells, molecules, and tissues. The role of mechanical force in various therapies, including microdeformating soft tissue techniques, shockwave, vacuum massage, tissue expansion, skin stretching and tension reducing therapies is the subject of numerous ongoing

clinical trials[27–30]. It can be assumed that many of the physical scar management methods, including compression therapy, silicone therapy, adhesive tape, and occlusive dressing therapy, are related to mechanotransduction mechanisms.

The non-invasive treatment or standard of care for scars post burn involves pressure therapy and silicone. Although treatment options, recommendations[31] and pathophysiology of the treatment options[32] have been described, the physical therapeutic effects on patients with scars remain poorly studied.

Practical and clinical implications

Clinical implications: An overview

Drawn on the measures investigated in this dissertation (also see Appendix) an ICF form is provided in Figure 7-1. For the **evaluation** of the patient with post burn scars in a clinical setting this form cannot be considered as complete since it may lack other relevant assessments. It was set up to visualise the investigated measures in light of what may clinically be feasible. The different subjective and objective measures that can be evaluated during physical examination in the physical therapist's health care process are classified within the appropriate domains. For the subjective measures the POSAS together with the EQ-5D and the BSHS-B are incorporated since the EQ-5D seems more complementary to the BSHS-B (Chapter 4)[33]. These PROMS are easy to use in daily practice and cheap. If objective measures can be afforded the inclusion of colour and TEWL measurements are advised.

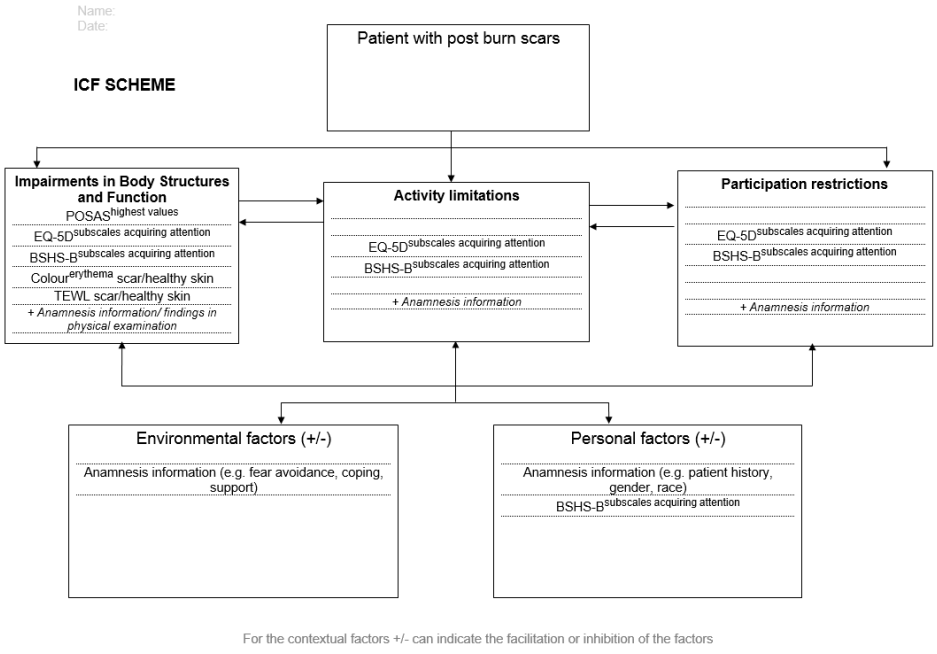

Figure 7-1 ICF form based on the investigated measures in this thesis applicable for evaluation of patients with post burn scars

This form is only a guide for testing in clinical aftercare settings and must be considered as a first step in directing biopsychosocial evaluation in post burn scar assessments and can be expanded with other objective assessments (e.g., pliability).

For the **treatment** of patients with post-burn scars a multidisciplinary approach seems in many occasions necessary due to the devastating impact on the patient. Drawn from the findings in this doctoral thesis the physical therapy treatment with vacuum massage can be considered besides pressure therapy and hydration to improve sensation.

Future research recommendations

In this doctoral thesis the focus was on evaluation and physical therapy treatment in patients with hypertrophic scars post burn, however, hypertrophic scarring occurs with high prevalence and high incidence (40-70%) after other surgical interventions[34]. Each year in the developed world a total of 100 million patients acquire scars as a results of selective surgery, surgery after trauma and burn injuries[35]. Several reviews are at hand[12,32,36–38] on non-invasive objective and subjective assessments of hypertrophic scars but few instruments have investigated physical features of scars across a variety of scar types[36]. The majority of the available literature on TEWL, colour and other scar measurement tools were tested on post burn scars[36]. How transferable these data would be on other scar types remains uncertain. The POSAS, the subjective scar scale which was used in this work, is also applicable for other scar types[39]. The generic HRQOL measures SF-36 and EQ-5D are well known within HRQOL research[4] and well-described within various other patient populations. When selecting HRQOL measures for clinical studies one can consider the ICF based comparison of the HRQOL measures to establish what should be measured. A combination of a generic measure and a specific measure is advised because the specific measures are often more responsive to change in that specific population[6,40]. The generic measures can capture comorbidities, allow comparison across conditions and are useful for cost-effectiveness analyses[41]. The BSHS-B, the burn specific measure investigated in this thesis, is not applicable for other patient populations. This led us to search for another disease specific measure. In patients with scars following injury or surgery, HRQOL can be assessed with the Dermatology Life Quality Index (DLQI)[42], a specific tool that showed promising results and significant differences in the impact on HRQOL between different scar type groups[43]. We would recommend to evaluate this specific DLQI against the EQ-5D and the BSHS-B similar to what was done with the BSHS-B in this thesis.

As already stated, the effect of non-invasive treatment for (non-burn) hypertrophic scars remains understudied. Several techniques for scars were proven to be effective through extensive

use[44] but no optimal treatment method is established[38]. Vacuum massage may prove its use beyond the burn population but needs to be investigated.

Future research recommendations for post-burn scar assessments:

- For future studies on TPT a force transducer should be included and multiple test procedures besides the 'ascending descending' procedure need to be investigated.
- Future research should try to establish cut-off values for change in POSAS items to determine the mean Clinically Important Differences.
- Since there are interactions between the different components of the ICF. This should be explored in future research. Can scar characteristics and scar quality (e.g., assessed with the POSAS) be linked or even predict activity limitations and participation restrictions evaluated by HRQOL subscales?
- Contextual Factors (environmental and personal) should be considered to be included in HRQOL measures. The findings in Chapter 4 indicate there is room for improvement regarding the burn specific instrument. Recently the EQ-5D was adapted to a five-level version[45,46] hence convergent validity may be higher and should be examined in further research. Also studies on the responsiveness of the different HRQOL measures in burn populations are recommended.

Future research recommendations for scar therapy effects:

- In comparative trials on vacuum massage or other physical therapy treatments different modalities on the broader impact (e.g., pliability thickness and HRQOL) should be incorporated in both short and long term follow-up. Homogeneity of groups should be guarded. The ideal intensity, duration, frequency and starting point for mechanical therapies should be evaluated to ensure remodeling of scars.
- Future research should concentrate on the investigation of the effects of physical therapy on scars beyond the post burn hypertrophic scars investigated in this thesis. These designs should take into account a larger sample size, power calculation, clear allocation in randomised studies and homogeneity.
- Since mechanical (e.g., shear stretching tension and compression) forces are perceived and received in the skin, investigation on the effects of postural stretching of the skin, shockwave

therapy and manual massage techniques should be considered in further investigations. The field of mechanobiology-based mechanotherapy is a promising field in medicine.

- Echographic images should be combined with histological examination to confirm the findings of vacuum massage on changes in epidermis and dermis.

General conclusion

This thesis highlights the validity and reliability of two objective devices -the SWMT to assess touch pressure threshold and the Scarbase Duo® to assess colour and TEWL- within the burn population. Moreover this thesis also evaluated the content and (convergent and discriminant) validity of commonly used HRQOL measures with the ICF to identify overlap. It evaluated the short-term effects of vacuum massage on epidermal and dermal structures and evaluated the long-term effects of vacuum massage on POSAS items pain, itch and TPT in addition to standard of care. Some of the investigated instruments, i.e. the EQ-5D (or the POSAS), are free and easy to use for research in rehabilitation settings. The assessment of TPT with the SWMT and colour and TEWL can be considered useful to measure specific objective characteristics of burn scars. The efficacy of vacuum massage (and manual therapy) for burn scar and scars in general is an issue still under debate, it is desirable that in the future increasing use be made of validated tools as outcome measures of the rehabilitation treatment. Studying the effects of vacuum massage on other function related scar characteristics such as elasticity are highly recommended. Despite its exploratory nature, this study offers some insight into mechanotherapy within physical therapy modalities.

Finally the ICF was presented as a useful framework to evaluate the content of PROMS, to look at the broad biopsychosocial impact of hypertrophic scars in burn patients. The aim of this thesis is to advocate the use of the ICF in post burn clinical evaluations and within research. The findings of this thesis have a number of important implications for future practice and research in post burn aftercare.

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SAMENVATTING

De huid, het grootste orgaan van het menselijk lichaam, en meer bepaald littekens na brandwonden zijn het topic van deze thesis. Het oplopen van brandwonden is een traumatische gebeurtenis die vaak gevolgd wordt door allerhande interventies gaande van acute tot langdurige multidisciplinaire nazorg. De kinesitherapeutische behandeling van littekens is een recente ontwikkeling waardoor er enerzijds bij de gezondheidswerker nog aan kennis ontbreekt aangaande dit topic en anderzijds de wetenschappelijke evidentie in de literatuur beperkt is.

Deze thesis focust op het dysfunctioneren van patiënten met littekens na brandwonden en gebruikt het International Classification of Functioning Disability and Health (ICF) als begrippenkader om de verschillende meetinstrumenten en vragenlijsten in dit werk te beschrijven. De inleiding van dit doctoraat verduidelijkt het ICF met de verschillende domeinen (Anatomische eigenschappen/Functies, Activiteiten en Participatie) en de problematiek gepaard gaande met de littekens na brandwonden. Vervolgens worden verschillende mogelijke meetinstrumenten alsook de fysiotherapeutische behandelingen toegelicht.

De kwaliteit van bestaande objectieve meetinstrumenten en kwaliteit van leven vragenlijsten voor patiënten met littekens na brandwonden werd besproken in deel 1 met daarin 4 verschillende hoofdstukken. In Hoofdstuk 1 werd de betrouwbaarheid van de Semmes Weinstein monofilament test (SWMT) aan de hand van de 'Ascending-Descending' methode onderzocht om de gevoelsdrempel (TPT) van de littekenhuid te meten. De resultaten toonde een goede intra-beoordeelaars betrouwbaarheid voor littekens na brandwonden alsook een goede betrouwbaarheid tussen twee beoordelaars. Hoofdstuk 2 onderzocht net zoals in Hoofdstuk 1 een meetinstrument voor het meten van functiestoornissen (eerste domein van het ICF) . De Scarbase Duo®, een recent ontwikkeld compact combinatie toestel voor het meten van kleur en waterdoorlaatbaarheid, bleek valide en betrouwbaar voor herhaalde metingen en ook tussen beoordelaars in de brandwonden populatie.

In Hoofdstuk 3 werd eerst gezocht naar de 3 meest gebruikte kwaliteit van leven (Quality of Life: QOL) vragenlijsten voor patiënten met brandwonden. De Burn Specific Health Scale Brief (BSHS-B) bleek de meest gebruikte ziekte specifieke QOL vragenlijst. De Short Form 36-items (SF-36) en de Euroqol 5 Dimensions (EQ-5D) bleken de meest beschreven generieke QOL vragenlijsten. Deze vragenlijsten werden inhoudelijk aan de hand van hun subschalen geclassificeerd binnen het ICF. Er bleek overeenstemming binnen verschillende ICF domeinen. De BSHS-B bleek de meeste ICF domeinen te coveren, had 5 unieke subschalen en bleek als enige vragenlijst persoonlijke factoren te

incorporeren. De SF-36 had slechts één unieke subschaal. Omgevingsfactoren werden in géén van de vragenlijsten beschreven. Deze theoretische classificatie binnen het ICF en de veronderstelde overeenstemming werd empirisch onderzocht in Hoofdstuk 4. De convergente validiteit bleek het hoogst tussen de generieke vragenlijsten (EQ-5D en SF-36). Bij het bekijken van de discriminant validiteit (verschil in groepen op basis van aantal operaties) hadden de generieke vragenlijsten een betere discriminant validiteit dan de BSHS-B. De studie toonde aan dat een korte generieke schaal reeds interessante informatie kan verschaffen over het dysfunctioneren, maar dient gecombineerd te worden met een uitgebreidere ziekte specifieke schaal om een vollediger beeld te krijgen. De meest gebruikte schalen om dysfunctioneren in kaart te brengen slagen er tot op heden niet in om de volledige impact na brandwonden te meten.

In deel 2 werden de effecten van vacuüm massage op het eerste domein van het ICF (Anatomische Eigenschappen en Functies) besproken. De effecten van vacuüm massage op pijn, jeuk en TPT (functiestoornissen) werden onderzocht via een vergelijkende studie in Hoofdstuk 5. Een groep die standaard nazorg ontving werd vergeleken met een groep die als additief vacuüm massage kreeg. Voor de vergelijking over tijd tussen de twee groepen konden geen significante verschillen worden aangetoond. Voor de vergelijking over tijd binnen de groep bleek significante verbetering voor TPT in de vacuüm massage groep. Pijn bleek significant verbeterd te zijn voor beide groepen; terwijl jeuk significant verbeterde in de standaard therapie groep. De korte termijn effecten op Anatomische eigenschappen; namelijk epidermale dikte en densiteit, werd aan de hand van ultrasonografie beschreven in Hoofdstuk 6. De mogelijke rol van vacuüm massage als vorm van mechanotherapie werd beschreven. Direct na de toepassing van vacuüm massage bleek een significante verandering in de epidermale densiteit. Bovendien werd een significante verandering in de dermale densiteit gevonden direct na alsook 2 u na toepassing van de therapie. De resultaten van dit onderzoek suggereren dermale remodelering.

Deze thesis illustreert het gebruik van het ICF binnen klinische evaluaties alsook in onderzoek voor patiënten met littekens na brandwonden. De effecten van vacuüm massage (en manuele therapie) voor deze patiënten vragen verder onderzoek met focus op meerdere uitkomstparameters (bijvoorbeeld de effecten op elasticiteit en de impact op QOL). Enkele inzichten voor mechanotherapie binnen kinesitherapeutische behandelingsmodaliteiten worden aangereikt en aanknopingspunten voor toekomstig onderzoek worden gegeven.

SUMMARY

The skin, the largest organ of the human body, and more specific post burn scars are the topic of this thesis. A burn injury is a traumatic event followed by a variety of interventions from acute care to multidisciplinary aftercare. Physical therapy for scars is a relatively new treatment modality, lacking knowledge amongst health care practitioners and evidence based therapy.

This thesis focusses on the post-burn dysfunctioning of patients with hypertrophic scars and used the International Classification of Functioning Disability and Health (ICF) framework to describe the different assessment tools and questionnaires. The general Introduction of this thesis illustrates the ICF with the different domains (Body Structures/Body Function, Activity, Participation) as well as the broad impact of post burn scars on patients. The different assessment measures and the physical treatments are introduced.

The quality of various ways to evaluate burn scars were addressed in Part 1 of this thesis. Four chapters are included. The first chapter elaborates on the reliability of the Semmes Weinstein monofilament test (SWMT) with the 'Ascending Descending' method to assess the touch pressure threshold in burn scars. Both interrater and intrarater reliability was shown for upper extremities burn scars and healthy subjects. Chapter 2 is a study investigating both reliability and validity of a dual assessment tool to measure TEWL and colour. The Scarbase Duo® a new, compact and affordable device was shown to be valid and reliable for repeated measures and between 2 raters. In the third chapter the most frequently used Health Related Quality of Life questionnaires were sought. The Burn Specific Health Scale-Brief (BSHS-B), the Short Form-36 items and the European Quality of Life 5 Dimensions (EQ-5D) were by the content of their subscales classified within the ICF framework. Overlaps and gaps were explored and revealed that the BSHS-B covered most ICF domains, had 5 unique subscales and was the only to include Personal Factors. The SF-36 had one unique subscale and none of the measures addressed contextual factors. This theoretical exercise was empirically evaluated in Chapter 4 with a prospective multicentre study. High convergence was shown between the generic measures (EQ-5D and SF-36). The EQ-5D and the SF-36 showed better discriminant validity than the BSHS-B across burn severity groups defined by the number of surgeries. This study illustrated that a short generic scale can provide interesting information but should be combined with a more comprehensive condition-specific scale in order to capture the full impact. Overall, this study supports the view that currently the most frequently used scales to measure functioning fall short to measure the full impact of a burn injury.

Part 2 of this thesis elaborated on the effects of vacuum massage on Body Structures and Body Functions. In Chapter 5 a comparative study between a usual care group and an intervention group receiving vacuum massage investigated the effects on pain, itch and TPT. Between-group analyses revealed no statistically significant differences between the groups over time. Within-group analysis for pain revealed a statistically significant improvement over time for both groups. A significant improvement for TPT was found in the intervention group, for itch the usual care group showed a statistically significant improvement. The short-term effects on Body structures; epidermal and dermal thickness and density assessed with high-frequency ultrasound scanning, were investigated in Chapter 6. Moreover the possible role of vacuum massage as a form of mechanotherapy was described. Significant changes in the epidermal density were found immediately after application and dermal density decreased after application and was still present after two hours. The results suggest that this the vacuum massage may lead to dermal extracellular matrix remodelling.

This thesis illustrated the use of the ICF to evaluate the content of Patient Reported Outcome Measures and advocates its use in post burn clinical evaluations and within research. The effects of vacuum massage (and manual therapy) on burn scars and scars in general is an issue still under debate. The effects of vacuum massage on quality of life and other scar characteristics such as elasticity requires further research. Despite its exploratory nature, this study offers some insights into mechanotherapy within physical therapy modalities. The findings of this thesis have a number of important implications for future practice and research in post burn aftercare.

Appendix

POSAS Patient scale

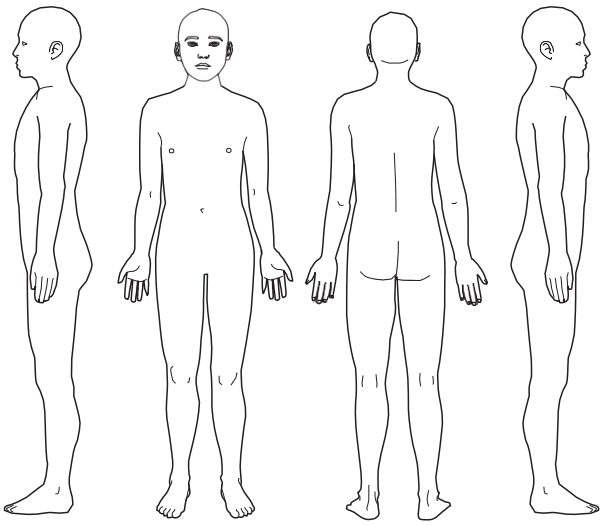
The Patient and Observer Scar Assessment Scale v 2.0 / NL

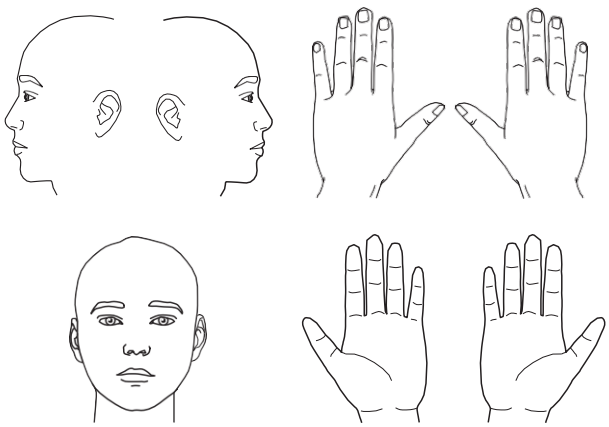
Datum onderzoek: _____ **Naam:** _____

Beoordelaar: _____

Locatie: _____ **Geboortedatum:** _____

Studie: _____ **Patientennummer:** _____





	1 = nee, helemaal niet … ja, heel erg = 10
	1 2 3 4 5 6 7 8 9 10
was het litteken de afgelopen weken pijnlijk?	○ ○ ○ ○ ○ ○ ○ ○ ○ ○
heeft het litteken gejeukt de afgelopen weken?	○ ○ ○ ○ ○ ○ ○ ○ ○ ○

	1 = nee, als normale huid … ja, het ergst denkbare verschil = 10
	1 2 3 4 5 6 7 8 9 10
is de kleur van het litteken op dit moment anders dan uw normale huid?	○ ○ ○ ○ ○ ○ ○ ○ ○ ○
is de stugheid van het litteken op dit moment anders dan uw normale huid?	○ ○ ○ ○ ○ ○ ○ ○ ○ ○
is de dikte van het litteken op dit moment anders dan uw normale huid?	○ ○ ○ ○ ○ ○ ○ ○ ○ ○
is het litteken op dit moment hobbeliger dan uw normale huid?	○ ○ ○ ○ ○ ○ ○ ○ ○ ○

	1 = Mooist mogelijke litteken … Lelijkst denkbare litteken = 10
	1 2 3 4 5 6 7 8 9 10
wat is uw algemene indruk van het litteken op dit moment?	○ ○ ○ ○ ○ ○ ○ ○ ○ ○

POSAS Observer scale

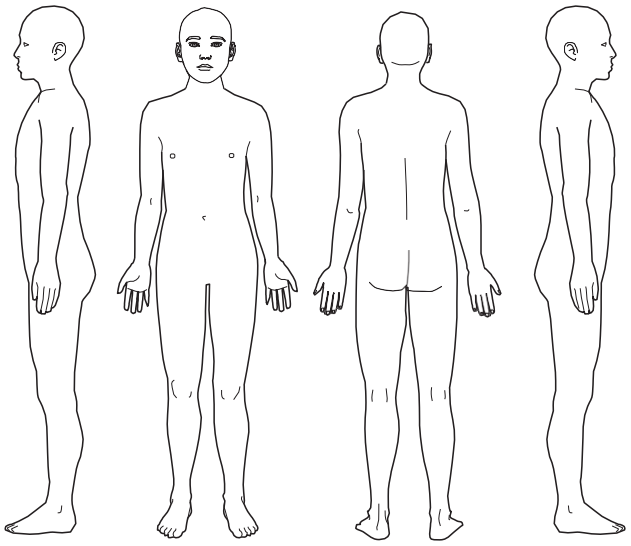
The Patient and Observer Scar Assessment Scale v 2.0 / NL

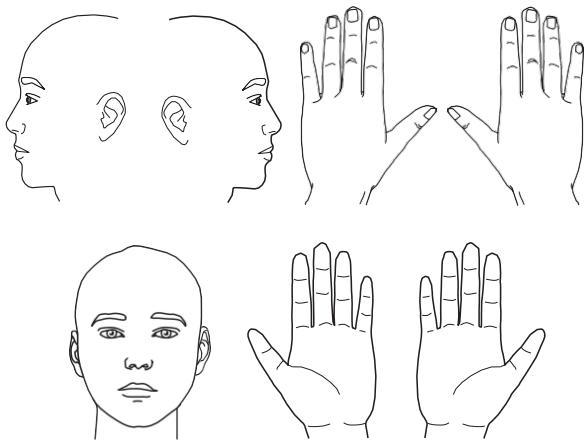
Datum onderzoek: _____ **Naam:** _____

Beoordelaar: _____

Locatie: _____ **Geboortedatum:** _____

Studie: _____ **Patientennummer:** _____





1 = normale huid **ergst denkbare litteken = 10**

parameter	1	2	3	4	5	6	7	8	9	10	categorie
vascularisatie											bleek | roze | rood | paars | mix
pigmentatie											hypo | hyper | mix
dikte											dikker| dunner
reliëf											vlakker | hobbeliger | mix
plooibaarheid											stugger | soepeler | mix
oppervlakte											expansie | contractie| mix
algehele indruk											

Toelichting

De POSAS bestaat uit de zes items (vascularisatie, pigmentatie, dikte, reliëf, plooibaarheid en opper- vlak) waarvan het litteken gescoord wordt op een schaal van 1 (als normale huid) tot 10 (als de ergste denkbare afwijking). De score van deze zes items resulteert in de 'POSAS totaal score'. Achter elk van de zes items staan categorieën vermeld die ingevuld kunnen worden. Daarnaast wordt de algemene indruk gescoord op een schaal van 1 tot 10.
Voor alle parameters geldt dat indien mogelijk een vergelijking dient plaats te vinden met normale huid op een overeenkomstige anatomische locatie.

Toelichting op de items:

• **vascularisatie** De vascularisatie wordt beoordeeld aan de hand van wegdrukbare roodheid. Dit wordt getest door met Plexiglas voldoende druk aan te brengen om de vaten in het litteken dicht te drukken en vervolgens het Plexiglas los te laten.
• **pigmentatie** De mate van bruine verkleuring van het litteken door de aan- of afwezigheid van melanine. Het plexiglas wordt tijdelijk op het litteken aangebracht met voldoende druk om de vaten in het litteken dicht te drukken waardoor de pigmentatie beter beoordeeld kan worden.
• **dikte** De gemiddelde afstand tussen de overgang subcutis – dermis en de epidermale oppervlakte van het litteken.
• **reliëf** De mate waarin oppervlakte onregel- matigheden van het litteken aanwezig zijn (Indien mogelijk wordt dit vergeleken met normale huid op een overeenkomstige anatomische locatie).
• **plooibaarheid** De soepelheid van het litteken. Dit wordt getest door de littekenhuid tussen duim en wijsvinger te plooien.
• **oppervlakte** De oppervlakte van het litteken in relatie tot het oorspronkelijke wondgebied.

Brandwond Specifieke Gezondheidsschaal

Naam: .....

Datum: ……

INSTRUCTIE

Deze vragenlijst gaat over problemen, klachten of gevoelens die sommige mensen ondervinden na het oplopen van brandwonden.

Er zijn vijf mogelijke antwoorden voor elke vraag. Deze zijn aangegeven bovenaan elke pagina.

Lees zorgvuldig elke vraag en duidt één antwoord aan dat in het algemeen het best bij u past of dat het beste omschrijft hoe u zich voelt.
Wij vragen u geen vragen over te slaan.

De vragen zijn uitspraken gedaan door andere mensen. Een voorbeeld hiervan is:

	heel veel	tamelijk veel	nogal	een beetje	helemaal niet
Ik heb veel last van jeuk.	☒	☐	☐	☐	☐

Denk niet te lang na over een antwoord!

Hoeveel moeite hebt u met:

		heel veel	tamelijk veel	nogal	een beetje	helemaal niet
1	Zelfstandig baden?	☐	☐	☐	☐	☐
2	Zelf aankleden?	☐	☐	☐	☐	☐
3	Gaan zitten in of opstaan uit een stoel?	☐	☐	☐	☐	☐
4	Uw naam schrijven?	☐	☐	☐	☐	☐
5	Zelfstandig eten?	☐	☐	☐	☐	☐
6	Schoenveters strikken, voorover buigen enz.?	☐	☐	☐	☐	☐
7	Oppakken van munten van een glad oppervlak?	☐	☐	☐	☐	☐
8	Openmaken van deuren?	☐	☐	☐	☐	☐
9	Werken in de oude functie en uitvoeren van de oude taken?	☐	☐	☐	☐	☐

In welke mate herkent u zich in de volgende uitspraken?

		heel veel	tamelijk veel	nogal	een beetje	helemaal niet
10	Soms zou ik willen vergeten dat mijn uiterlijk is veranderd.	☐	☐	☐	☐	☐
11	Ik voel dat mijn brandwond anderen afschrikt.	☐	☐	☐	☐	☐
12	Ik heb last van het gevoel van eenzaamheid.	☐	☐	☐	☐	☐
13	Ik voel me vaak verdrietig en teneergeslagen.	☐	☐	☐	☐	☐

		heel veel	tamelijk veel	nogal	een beetje	helemaal niet
14	Soms denk ik zelf dat ik een emotioneel probleem heb.	☐	☐	☐	☐	☐
15	Ik ben niet geïnteresseerd in activiteiten met vrienden.	☐	☐	☐	☐	☐
16	Ik vind het niet leuk bij mensen op bezoek te gaan.	☐	☐	☐	☐	☐
17	Door mijn verwonding is er een afstand tussen mij en mijn gezin ontstaan.	☐	☐	☐	☐	☐
18	Ik ben liever alleen dan bij mijn familie.	☐	☐	☐	☐	☐
19	Ik vind het vervelend zoals mijn familie reageert als ik er bij ben.	☐	☐	☐	☐	☐
20	Mijn gezin is beter af zonder mij.	☐	☐	☐	☐	☐
21	Ik kan met niemand over mijn problemen praten.	☐	☐	☐	☐	☐
22	Ik voel me gefrustreerd omdat ik niet seksueel opgewonden raak zoals vroeger.	☐	☐	☐	☐	☐
23	Ik ben gewoon niet meer zo geïnteresseerd in seks.	☐	☐	☐	☐	☐
24	Ik omhels, knuffel of zoen niet meer.	☐	☐	☐	☐	☐
25	Ik heb echt last van mijn uiterlijk.	☐	☐	☐	☐	☐
26	Ik heb het gevoel klem te zitten of te zijn opgesloten.	☐	☐	☐	☐	☐

De volgend vragen gaan over gevoeligheid en verzorging van de brandwond. In welke mate herkent u zich in de volgende uitspraken?

		heel veel	tamelijk veel	nogal	een beetje	helemaal niet
27	Ik vind het vervelend om buiten in de zon te zijn.	☐	☐	☐	☐	☐
28	Ik heb last van warm weer.	☐	☐	☐	☐	☐
29	Ik kan met warm weer niet naar buiten om iets te doen.	☐	☐	☐	☐	☐
30	Ik vind het vervelend dat ik niet buiten in de zon kan zijn.	☐	☐	☐	☐	☐
31	Mijn huid is gevoeliger geworden.	☐	☐	☐	☐	☐
32	De verzorging van mijn huid is een last.	☐	☐	☐	☐	☐
33	Er zijn dingen die ik moet doen voor de verzorging van mijn brandwond die ik vervelend vind.	☐	☐	☐	☐	☐
34	Ik wilde dat ik niet zoveel moest doen bij de verzorging van mijn brandwond.	☐	☐	☐	☐	☐
35	Ik heb moeite met alle dingen die ik moet doen voor de verzorging van mijn brandwond.	☐	☐	☐	☐	☐
36	De verzorging van mijn brandwond maakt het moeilijk andere dingen te doen die ik belangrijk vind.	☐	☐	☐	☐	☐
37	Mijn brandwond stoort mij bij mijn werk.	☐	☐	☐	☐	☐
38	Verbrand zijn heeft mijn prestaties verminderd.	☐	☐	☐	☐	☐
39	Mijn brandwond heeft problemen veroorzaakt met mijn functioneren.	☐	☐	☐	☐	☐
40	Ik vind mijn littekens er hinderlijk uitzien.	☐	☐	☐	☐	☐

SF-36 GEZONDHEIDSTOESTAND VRAGENLIJST

INSTRUCTIE: Deze vragenlijst gaat over uw standpunten t.a.v. uw gezondheid. Met behulp van deze gegevens kan worden bijgehouden hoe u zich voelt en hoe goed u in staat bent uw gebruikelijke bezigheden uit te voeren.

Beantwoord elke vraag door het antwoord op de aangegeven wijze te markeren. Als u niet zeker weet hoe u een vraag moet beantwoorden, geef dan het best mogelijke antwoord.

1. Hoe zou u over het algemeen uw gezondheid noemen?

(omcirkel één cijfer)

Uitstekend	1
Zeer goed	2
Goed	3
Matig	4
Slecht	5

2. Hoe beoordeelt u nu uw gezondheid over het algemeen, vergeleken met een jaar geleden?

(omcirkel één cijfer)

Veel beter nu dan een jaar geleden	1
Wat beter nu dan een jaar geleden	2
Ongeveer hetzelfde nu als een jaar geleden . . .	3
Wat slechter nu dan een jaar geleden	4
Veel slechter nu dan een jaar geleden	5

3. De volgende vragen gaan over bezigheden die u misschien doet op een doorsnee dag. Wordt u door uw gezondheid op dit moment beperkt bij deze bezigheden? Zo ja, in welke mate?

(omcirkel één cijfer op elke regel)

BEZIGHEDEN	Ja, ernstig beperkt	Ja, een beetje beperkt	Nee, hele-maal niet
a. Forse inspanning, zoals hardlopen, tillen van zware voorwerpen, een veeleisende sport beoefenen	1	2	3
b. Matige inspanning, zoals een tafel verplaatsen, stofzuigen, zwemmen of fietsen	1	2	3
c. Boodschappen tillen of dragen	1	2	3
d. Een paar trappen oplopen	1	2	3
e. Eén trap oplopen	1	2	3
f. Bukken, knielen of hurken	1	2	3
g. Meer dan een kilometer lopen	1	2	3
h. Een paar honderd meter lopen	1	2	3
i. Ongeveer honderd meter lopen	1	2	3
j. Uzelf wassen of aankleden	1	2	3

4. Heeft u in de afgelopen 4 weken, een van de volgende problemen bij uw werk of andere dagelijkse bezigheden gehad, ten gevolge van uw lichamelijke gezondheid?

(omcirkel één cijfer op elke regel)

	JA	NEE
a. U besteedde minder tijd aan werk of andere bezigheden	1	2
b. U heeft minder bereikt dan u zou willen	1	2
c. U was beperkt in het soort werk of andere bezigheden	1	2
d. U had moeite om uw werk of andere bezigheden uit te voeren (het kostte u bv. extra inspanning)	1	2

5. Heeft u in de afgelopen 4 weken, een van de volgende problemen ondervonden bij uw werk of andere dagelijkse bezigheden ten gevolge van emotionele problemen (zoals depressieve of angstige gevoelens)?

(omcirkel één cijfer op elke regel)

	JA	NEE
a. U besteedde minder tijd aan werk of andere bezigheden	1	2
b. U heeft minder bereikt dan u zou willen	1	2
c. U deed uw werk of andere bezigheden niet zo zorgvuldig als gewoonlijk	1	2

6. In hoeverre hebben uw lichamelijke gezondheid of emotionele problemen u gedurende de afgelopen 4 weken gehinderd in uw normale omgang met familie, vrienden of buren, of bij activiteiten in groepsverband?

(omcirkel één cijfer)

Helemaal niet 1

Enigszins 2

Nogal 3

Veel 4

Heel erg veel 5

7. Hoeveel lichamelijke pijn heeft u de afgelopen 4 weken gehad?

(omcirkel één cijfer)

Geen 1

Heel licht 2

Licht 3

Nogal 4

Ernstig 5

Heel ernstig 6

8. In welke mate bent u de afgelopen 4 weken door pijn gehinderd in uw normale werk (zowel werk buitenshuis als huishoudelijk werk)?

(omcirkel één cijfer)

Helemaal niet 1

Een klein beetje 2

Nogal 3

Veel 4

Heel erg veel 5

9. Deze vragen gaan over hoe u zich voelt en hoe het met u ging in de afgelopen 4 weken. Wilt u a.u.b. bij elke vraag het antwoord geven dat het best benadert hoe u zich voelde. Hoe vaak gedurende de afgelopen 4 weken

(omcirkel één cijfer op elke regel)

	altijd	meestal	vaak	soms	zelden	nooit
a. Voelde u zich levenslustig?	1	2	3	4	5	6
b. Was u erg zenuwachtig?	1	2	3	4	5	6
c. Zat u zo in de put dat niets u kon opvrolijken?	1	2	3	4	5	6
d. Voelde u zich rustig en tevreden?	1	2	3	4	5	6
e. Had u veel energie?	1	2	3	4	5	6
f. Voelde u zich somber en neerslachtig?	1	2	3	4	5	6
g. Voelde u zich uitgeput?	1	2	3	4	5	6
h. Was u een gelukkig mens?	1	2	3	4	5	6
i. Voelde u zich moe?	1	2	3	4	5	6

10. Hoe vaak hebben uw lichamelijke gezondheid of emotionele problemen u gedurende de afgelopen 4 weken gehinderd bij uw sociale activiteiten (zoals vrienden of familie bezoeken, etc)?

(omcirkel één cijfer)

Altijd	1
Meestal	2
Soms	3
Zelden	4
Nooit	5

11. Hoe JUIST of ONJUIST is elk van de volgende uitspraken voor u?

(omcirkel één cijfer op elke regel)

	volkomen juist	grotendeels juist	weet ik niet	grotendeels onjuist	volkomen onjuist
a. Ik lijk wat gemakkelijker ziek te worden	1	2	3	4	5
b. Ik ben even gezond als andere mensen	1	2	3	4	5
c. Ik verwacht dat mijn gezondheid achteruit zal gaan	1	2	3	4	5
d. Mijn gezondheid is uitstekend	1	2	3	4	5

Gezondheidsvragenlijst

Nederlandse versie voor België

(Dutch version for Belgium)

Zet bij iedere hieronder vermelde groep een kruisje in één hokje achter de zin die het best uw gezondheidstoestand van vandaag weergeeft.

Mobiliteit

Ik heb geen problemen met rondwandelen	D
Ik heb enige problemen met rondwandelen	D
Ik ben bedlegerig	D

Zelfzorg

Ik heb geen problemen om voor mezelf te zorgen	D
Ik heb enige problemen om mezelf te wassen of aan te kleden	D
Ik ben niet in staat mezelf te wassen of aan te kleden	D

Dagelijkse activiteiten *(bijv. werk, studie, huishouden, gezins- of vrijetijdsactiviteiten)*

Ik heb geen problemen met mijn dagelijkse activiteiten	D
Ik heb enige problemen met mijn dagelijkse activiteiten	D
Ik ben niet in staat mijn dagelijkse activiteiten uit te voeren	D

Pijn/klachten

Ik heb geen pijn of andere klachten	D
Ik heb matige pijn of andere klachten	D
Ik heb zeer ernstige pijn of andere klachten	D

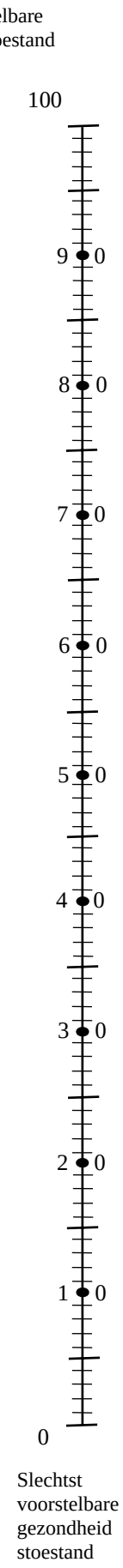
Angst/depressie

Ik ben niet angstig of depressief	D
Ik ben matig angstig of depressief	D
Ik ben erg angstig of depressief	D

Om mensen te helpen bij het aangeven hoe goed of hoe slecht een gezondheidstoestand is, hebben we een meetschaal (te vergelijken met een thermometer) gemaakt. Op de meetschaal hiernaast betekent “100” de beste gezondheidstoestand die u zich kunt voorstellen, en “0” de slechtste gezondheidstoestand die u zich kunt voorstellen.

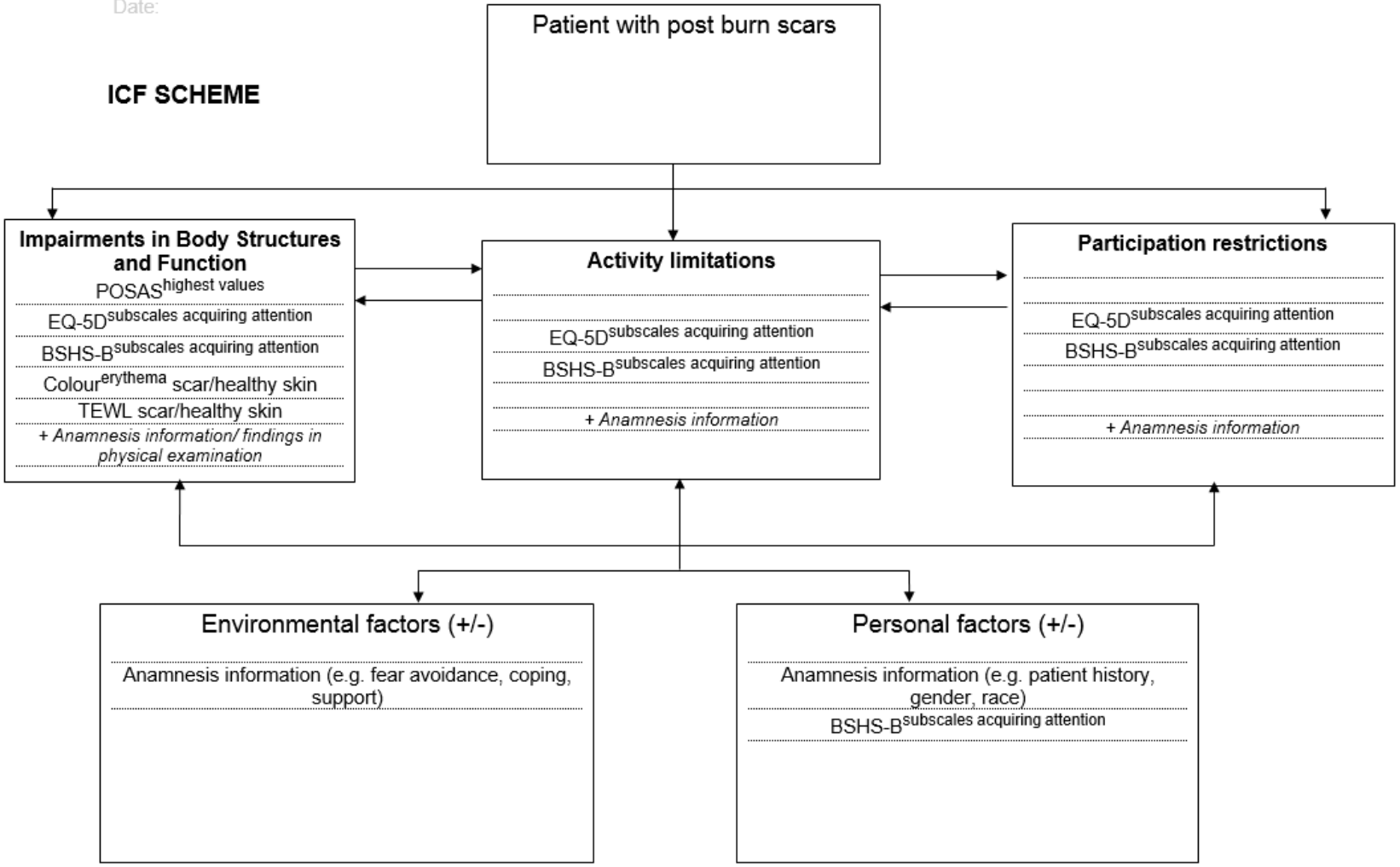
We willen u vragen op deze meetschaal aan te geven hoe goed of hoe slecht volgens u uw eigen gezondheidstoestand vandaag is. Trek een lijn van het hokje hieronder naar het punt op de meetschaal dat volgens u aangeeft hoe goed of hoe slecht uw gezondheidstoestand vandaag is.

Uw gezondheidstoestand vandaag



Name:
Date:

ICF SCHEME



For the contextual factors +/- can indicate the facilitation or inhibition of the factors

Curriculum vitae

Personalia
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 @jillmeirte

Education
Master in Physiotherapy, Cum Laude, Hogeschool Antwerpen, 2004

Employments
Physiotherapist in WZC De Regenboog, 2004 - 2005
Physiotherapist in private practices, 2004 - 2006
Head of physical therapy and occupational therapy team (PT and OT team) in WZC De Regenboog, 2005 - 2009
Assistant Rehabilitation Sciences and Physiotherapy, University of Antwerp, Department of Rehabilitation Sciences and Physiotherapy 2009 - present
Research fellow, Oscare Scar After-Care and Research Centre, 2012 - present

Research activities
Researcher within Scientific Research Project G848 "Onderzoek naar determinanten en management van fysieke activiteiten van chronisch vermoeide personen genezen van kanker en van individuen met het chronisch vermoeidheid syndroom", 2009-2012
PhD in cooperation with Oscare 2012-present

Conference and symposia presentations
2012
- The effects of PRUS® depressomassage on pain, pruritus and sensory perception in burn scars. Meirte J, Moortgat P, Van Daele U, Maertens K, Vaneerdeweg W. Oral presentation for the 4th International Scar Club Congress, Faculty of Medicine, 22-24 march 2012, Montpellier, France.
- The effects of vacuummassage on pain, pruritus and sensory perception in burn scars. Meirte J, Anthonissen M, De Cuyper L, Van Daele U, Moortgat P, Maertens K, Vaneerdeweg W. Oral presentation at the International Society for Burn Injury congres, 9-13 september 2012, Edinburgh, Scotland
- Functionele outcome bij brandwonden en littekens in relatie tot het ICF.Course at the Physioburn Symposium, 9 november 2012 in CHU Luik.

2013
- Kwaliteit van leven vragenlijsten bij patiënten met brandwonden: wat meten we (niet)? Meirte J, Van Loey N, Maertens K, Moortgat P, Hubens G, Van Daele U. Oral presentation at voorjaars symposium van de Nederlandse Vereniging voor Brandwonden Zorg op 5 april 2013 in Merksem.
- The effects of depressomassage on color in burns. Anthonissen M, Meirte J, Moortgat P, Lafaire C, Maertens K. Oral presentation at the 15th European Burn Association Congress. August 28th-31st 2013, Vienna, Austria.
- Can a cohesive compressive silicone bandage outperform silicone gel sheets in the treatment of burn scars? A preliminary report. Moortgat P, Anthonissen M, Meirte J, Lafaire C, Maertens

K. Oral presentation at the 15th European Burn Association Congress. August 28th-31st 2013, Vienna, Austria.

- Is the Semmes Weinstein aesthesiometer a reliable instrument for determining tactile sensitivity in patients with burns and matched controls? Meirte J, Meir S, De Cuyper L, Lafaire C, Moortgat P, Maertens K, Hubens G, Van Daele U. Oral presentation at the 15th European Burn Association Congress. August 28th-31st 2013, Vienna, Austria.
- To know or not to know…when measuring quality of life in patients with burns. Meirte J, Van Loey N, Maertens K, Moortagt P, Hubens G, Van Daele U. Oral presentation at the 15th European Burn Association Congress. August 28th-31st 2013, Vienna, Austria.
- Behandel (on)mogelijkheden van endermotherapie. Invited speaker at the annual Conference voor Huidtherapeuten, 2 november 2013, Ede, The Netherlands.

2014

- Objective Scar Measurements. Workshop at SCARACADEMY UK in Birmingham, 14 june 2014
- Quality of Life and ICF. lecture at SCARACADEMY UK in Birmingham,14 june 2014
- Clinimetric properties of a new pressure algometer to evaluate pressure pain threshold in patients with burn scars. Meirte J, Meir S, De Cuyper L, Lafaire C, Moortgat P, Maertens K, Hubens G, Van Daele U. Oral presentation at ISBI congress 2014, 16 october 2014, Sydney Australië
- Physical scar management. Opleiding Littekentherapie-Scaracademy op 8 november 2014 op campus Drie Eiken.

2015

- ICF en littekens en Clinical Assessments bij littekens. Lectures in de Kinesitherapeutische Workshop Littekentherapie Manuele technieken en Depressomassage op 21 maart 2015.
- The Short-term effects of vacuummassage on thickness and density of burns scars. Meirte J, Athonissen M, Temmerman S, Lafaire C, De Cuyper L, Maertens K, Moortgat P. Van Daele U, Hubens G. Oral presentation at the 16th European Burn Association Congress, 16 september 2015, Hannover, Germany.
- Silicon gel shets in the treatment of burn scars: final results of a randomised comparitive study. Moortgat P, Anthonissen M, Meirte J, Lafaire C, De Cuyper L, Maertens K. A Cohesive compressive silicone bandage vs. Oral presentation at the 16th European Burn Association Congress, 16 september 2015, Hannover, Germany.
- Tension reducing taping as a mechanotherapy for hypertrophic burn scars- a proof of concept.Moortgat P, Van Daele U, Anthonissen M, Meirte J, Lafaire C, De Cuyper L, Maertens K.Oral presentation at the 16th European Burn Association Congress, 16 september 2015, Hannover, Germany.
- Intrarater and interrater reliability of an open 22MHz Ultrasaound scanning system to assess thickness and density of burn scars. Anthonissen M, Meirte J, Moortgat P, Temmerman S, Lafaire C, De Cuyper L, Maertens K. Oral presentation at the 16th European Burn Association Congress, 16 september 2015, Hannover, Germany.
- Extracorporeal shockwave therapy for the management of hypertrophic scars: preiminary results of a randomised placebo controlled trial. Moortgat P, Meirte J, Anthonissen M, De Cuyper L, Lafaire C, Maertens K. Oral presentation at the 16th European Burn Association Congress, 16 september 2015, Hannover, Germany.
- Scar severity and quality of life: an obvious relationship. Meirte J, Van Daele U, Mortgat P, Van Loey N, Maertens K, Hubens G. Oral presentation at the 16th European Burn Association Congress, 16 september 2015, Hannover, Germany.
- A reliabe, easy to use and portable device to monitor the scar healing process. Fell M, Meirte J, Anthonissen M, Peat J, Maertens K, Moortgat P. Oral presentation at the 16th European Burn Association Congress, 16 september 2015, Hannover, Germany.
- was reviewer for journals ‘Muscle and Nerve’ and ‘Quality of life research’.
- New theories in physical scar management for reduction of post burn scar hypertrophy. Van Daele U, Meirte J, Anthonissen M, Maertens K, Lafaire C, De Cuyper L, Moortgat P. Oral

presentation (invited speaker) at 2015 Annual Meeting of Chinese Burns Association. 4-7 November 2016. Shenzhen, China.

2016

- Physical Scar management. Moortgat P, Meirte J, Anthonissen M. Course 'Vasculaire kinesitherapie en oncologie postacademische vormingsreeks voor kinesitherapeuten', 23 april 2016, VUB, Brussels.
- Extracorporeal shockwave-therapy as an anti-scarring agent after delayed wound healing: Preliminary results of a randomised placebo controlled trial. Meirte J, Moortgat P, Anthonissen M, , Lafaire c, De Cuyper L, Maertens K. Oral presentation at EWMA, 11-13 May 2016, Bremen, Germany.
- Workshop Adaptive treatment pathways for scar pathologies with Oscare After-Care team, Scarcon conference, 3-4 june 2016, Antwerp.
- Scar severity and Quality of Life. Meirte J, Van Daele U, Moortgat P, Van Loey NE, Maertens K, Hubens G. Invited keynote lecture. Scarcon conference, 3-4 june 2016, Antwerp.
- The effects of shockwave therapy on burn scars: a randomised comparative trial. Meirte J, Moortgat P, Anthonissen M, Lafaire C, De Cuyper L, Maertens K. Oral presentation at Scarcon conference, 3-4 june 2016, Antwerp.

Prizes/Awards

- Professionals Allied to medicine (PAM) prize for best presentation with 'Is the Semmes Weinstein aesthesiometer a reliable instrument for determining tactile sensitivity in patients with burns and matched controls?' at the European Burn Association congress, August 2013, Vienna, Austria.
- Won subsidy 'Omkadering Jong Onderzoekers' for research stay abroad for the ISBI 2014 in Sydney
- Scar Severity and Quality of Life: An obvious relationship? Was nominated for the Kreisprijs in 2015 and won 3rd prize.

List of PhD related Publications

- Classification of Quality of life subscales within the ICF framework in burn research: identifying overlaps and gaps. Meirte J, van Loey NE, Maertens K, Moortgat P, Hubens G, Van Daele U. Burns. 2014; 40(7):1353-9.
- Interrater and intrarater reliability of the Semmes Weinstein aesthesiometer to assess touch pressure threshold in burn scars. Meirte J, Moortgat P, Truijen S, Maertens K, Lafaire C, De Cuyper L, Hubens G, Van Daele U. Burns 2015; 41 (6);1261-1267.
- The Scarbase Duo: Intra-rater and inter-rater reliability and validity of a compact dual scar assessment tool. Fell M, Meirte J, Anthonnissen M et al. Burns 2016; 42(2):336-44
- Short-term effects of vacuum massage on epidermal and dermal thickness and density in burn scars: an experimental study. Meirte J, Moortgat P, Anthonissen M, Maertens K, Lafaire C, De Cuyper L, Hubens G, Van Daele U. Burns and Trauma 2016; 4: 27.
- Convergent and discriminant validity of quality of life measures used in burn populations. Meirte J, Van Daele U, Maertens K, Moortgat P, Deleus R, Van Loey NE. Accepted for publication in Burns.
- The Physical and Physiological Effects of Vacuum Massage on the Different Skin Layers: A Current Status of the Literature. Moortgat P, Anthonissen M, Meirte J, Maertens K, Van Daele U. Accepted for publication in Burns and Trauma.

Other publications

- The effectiveness of physiotherapy for cervical dystonia: a systematic literature review. De Pauw J, Van der Velden K, Meirte J, Van Daele U, Truijen S, Cras P, Mercelis R, De Hertogh W. J Neurol. 2014 Oct;261(10):1857-65
- Activity pacing self-management in chronic fatigue syndrome: A randomized controlled trial. Kos D, van Eupen I, Meirte J, Van Cauwenbergh D, Moorkens G, Meeus M, Nijs J. 2015. American Journal of Occupational Therapy; 69(5):6905290020

- The effectiveness of a self-management occupational therapy intervention on activity performance in individuals with multiple sclerosis-related fatigue: a randomized-controlled trial. Kos D, Duportail M, Meirte J, Meeus M, D'hooghe MB, Nagels G, Willekens B, Meurrens T, Ilsbroukx S, Nijs J. Int J Rehabil Res. 2016 (article in press).

Teaching activities

University of Antwerp Artesis Hogeschool Antwerpen, 2009 – present

- Bachelor and Master of rehabilitation Sciences and Physiotherapy Education
- Co-supervisor of MSc dissertations (12 completed)

Courses

- Echo Assistentenopleiding 2011-2012
- Scar academy level of Knowledge 2011
- Scar academy level of Skills 2012
- Giving presentations in English 2012
- Linguapolis course writing academic paper in English 2013
- Masterclass wetenschapscommunicatie 2014
- Course/workshop presentatietechnieken 13/2/2014
- Statua course Basic principles in statistics 27/10-4/11/2014

Others

- Organisor Opencampusdag, Resonantiedag (Artesis opleiding Revaki), 2009-2012
- Secretary vakgroep Muskuloskeletale Kinesitherapie, 2009-2012
- Co-organisor Scarcon 2016 wetenschappelijk congres (03/06/2016 - 04/06/2016)
- Co-organisor permanente vorming "Scar Academy" (27/09/2014 - 29/11/2014)
- Member integratiepersoneelsonderhandelingscomité UA (2012 - present)
- Member Physioburn (2012 - present)
- Collaboration with Matt Fell (british medical doctor research stay in Belgium (combined research with Scarbase duo device)) in 2013
- Collaboration with Nederlandse Vereniging voor Brandwonden Zorg 2013- present

Dankwoord

Het doctoraat is af, dus werd het tijd om het dankwoord te schrijven.

Op de eerste plaats bedank ik graag alle patiënten die aan de onderzoeken meewerkten. Door jullie bijdrage en bereidwilligheid om al die testen te 'ondergaan' en de vragenlijsten in te vullen was het mogelijk om een beeld te krijgen over de kwaliteit van de verschillende instrumenten en van onze gegeven zorg en therapieën.

Daarnaast verdient iedereen van de collega's en vrijwilligers uit Oscare een welgemeende dank. Ik heb met ontzettend veel plezier de afgelopen jaren met jullie allen samengewerkt en heb me er steeds thuis en welkom mogen voelen. Dr. Lafaire en Dr. De Cuyper jullie zijn toppers, jullie zijn artsen, chirurgen met het hart op de juiste plaats. Onze patiënten zijn gezegend met jullie vakkundigheid maar bovenal met jullie warme zorg. Van mijn kine collega's Peter, Pascal, Yannick ,Jurgen, Mieke en Joni heb ik heel veel kunnen leren van hun klinische ervaringen met patiënten met brandwonden, ontzettend veel dank! Koen, nogmaals proficiat met het 15-jarige bestaan van Oscare. Bedankt voor de adviezen en het besturen van dit prachtige schip.

Peter, bij jou is heel dit verhaal begonnen. Jouw gedrevenheid en passie voor wetenschap en onderzoek werkt zo aanstekelijk. Voor alles kon ik bij jou terecht. Naast gids, beschermer en coach op de vele congressen, heb jij vanop de eerste lijn dit onderzoek mee vorm gegeven en gecoördineerd. Jij hebt dit mogelijk gemaakt en ik wil je daarvoor heel hartelijk bedanken. Merci!

Prof. Vaneerdeweg, bedankt voor uw begeleiding en steeds constructieve feedback in de opstart van dit doctoraat. Prof. Dr. Hubens, nog voor u mijn promotor werd, was u al iemand die ik eeuwig dankbaar zou blijven. U opereerde mijn zoontje Brent het jaar voor mijn doctoraat van start ging. Toen ik na het emiritaat van Prof. Vaneerdeweg vernam dat u zijn taak zou overnemen, was ik vereerd en dankbaar. Bij iedere meeting wist ik weer hoe ik verder kon, waar we aan konden werken en had ik weer nieuwe moed. Bedankt voor alle tijd die u in me investeerde. Je liet me vrij maar was er altijd met goede raad, adviezen en belangstelling.

Prof. Van Daele, Ulrike, ik ben heel blij dat je met die initiële vraag over onderzoek omtrent kinesitherapie bij brandwonden naar me toe bent gestapt. Ik wou onderzoek doen, maar moest iets vinden waar ik door kon worden gebeten en dat deed het zeker! Je hebt me ondersteund en begeleid met goede raad en adviezen. Je was voor mij een super promotor. Ik wil je ontzettend bedanken voor alles. Ik bewonder je als prof. in al wat je doet voor de opleiding en de vakgroep, maar ook als collega en vriendin. We hebben al veel onderwijs- en onderzoek gerelateerde mooie momenten gedeeld, maar ook daarbuiten hebben we menig maal gelachen en plezier gehad. Ik hoop dat we nog lang kunnen blijven samenwerken en nog kunnen uitgroeien wat betreft onderwijs en onderzoek omtrent littekens binnen de faculteit en hopelijk ook ver daarbuiten. Het samen deelnemen aan een internationaal congres, dat hou ik je nog te goed.

Geachte leden van de leescommissie, Prof. dr. Lambert, Prof. dr. Stassijns, Prof. Van den Kerckhove, Prof. dr. Van Zuijlen. Ik wil u hartelijk danken voor uw tijd om mijn manuscript te beoordelen en uw bereidheid om te zetelen in de jury.

Aan alle collega's van de REVAKI, werken met plezier en met plezierige mensen werken dat is een zegen. Willem, Greet, Patty, Christel, Deborah en Annette bedankt voor de vele fijne les- en examen momenten. In het bijzonder wil ik Annette bedanken. Jij hebt menig maal mijn onderwijstaken

opgevangen en sprong in de bres als ik het afgelopen academiejaar door onderzoekstaken alweer weinig tijd had voor onderwijsvoorbereidingen. Ik mocht in 2009 starten als jouw “buddy” voor de lesopdrachten en ben zo blij dat we nog steeds in duo de lessen basisonderzoek mogen verzorgen. Je was een luisterend oor, gaf me regelmatig goed advies en met jou samenwerken maakt me steeds gelukkig. Nick, bedankt dat ik binnen de lessen Vasculaire Pathologie de lessen rond brandwonden en littekens mag geven aan de studenten REVAKI. Kris en Sarah bedankt voor de tips rond het inbinden en verdedigen van een doctoraat. Christel, Wendy, Marijke, Kevin, Justien, Lenie, Evi, Joke, Hanne en alle anderen veel succes met het verderzetten van jullie doctoraat.

Lieve vrienden en familie, ik ben gezegend met jullie in mijn leven. Bedankt voor al die momenten van amusement en ontspanning. Ze zeggen wel eens ‘every blond needs a brunette’ wel ik heb een heel team van brunettes. Melissa, oneindig dikke merci voor alle berichtjes je aanmoedigingen, het meeleven en de steun doorheen al die jaren. Lenie, jij had zoveel vertrouwen in mij dat je zelfs een deel van je trouw door mij liet coördineren. Bedankt om zo in me te geloven en af en toe mijn zelfvertrouwen op te krikken. Ik wens je ontzettend veel succes met de verderzetting van je doctoraat. Ik geloof ook in u! Lieve Annick, bedankt voor de steun en vriendschap. Mieke, bedankt voor de vele leuke congresmomenten, jij bent voor eeuwig mijn room-mate. Pascale, al van kind af zie ik je als een grote zus die ik nooit heb gehad en waar ik met veel trots naar opkijk. Vele vakanties, uitstapjes en momenten met onze kindjes bewaar ik in mijn hart. Je was er altijd voor me ook als het tegenzat. Ellen, Milena en Erik, bedankt voor jullie belangstelling en vriendschap al sinds onze studententijd! Ook Marc, Yves, Cliff, Annelies, Guy, Patricia, Vincent en alle andere vrienden en familie, merci voor de uitstapjes, de lieve berichten en feestjes die me regelmatig de stress even lieten vergeten.

Matthias, jij hebt ook deze rollercoaster van dichtbij mogen ervaren of beter gezegd moeten ondergaan. Soms was ik moe, soms hyperkinetisch en overactief, soms met, dan weer zonder stress, je hebt ongetwijfeld al mijn alter ego’s al moeten doorstaan of er zelfs al die jaren mee ‘moeten’ dansen. Ik dank je van harte voor alles; de praatjes, de aanmoediging, de lieve facebook posts, maar bovenal voor al die uren dans die we samen al mochten beleven. Aan alle Showcarrousellers groot en klein bedankt voor de fijne tijd tijdens de dansrepetities en optredens. Ik ben blij dat ik jullie dansjuf mag zijn.

Gregory, lieve schat. Toen ik in 2012 de beslissing nam om te gaan doctoreren, wisten we allebei niet precies wat dat zou gaan betekenen. Met een klein hartje sprongen we in het diepe. Dat het af en toe woelige wateren waren dat heb jij mee mogen beleven. Maar af en toe konden we ook letterlijk en figuurlijk op het strand genieten van de zon. Samen met de jongens maken jullie mijn leven compleet. Ik wil je bedanken voor het geduld, het opvangen van de kinderen toen ik weer eens in het buitenland zat of me thuis had opgesloten om verder te werken. Soms was ik geen zonnetje in huis en zat mijn hoofd vol zorgen, maar iedere keer wist je me op te vrolijken en aan te moedigen. Je bent mijn steun en toeverlaat.
Xander, je bent een zorgzame, speelse, knappe kerel met veel interesse in wetenschap. Je nieuwsgierigheid, je eerlijkheid en je hart van goud zullen je nog ver brengen. Brent, je hebt al het een en het ander meegemaakt, maar je bent zo een sterke en zelfzekere kerel. Met je leergierigheid en doorzettingsvermogen zal je nog veel kunnen bereiken. Je maakte ons gezinnetje compleet. Mama haar boek is nu klaar en ik beloof geen enkel verjaardagsfeestje meer te missen. Mama en papa geloven heel sterk in jullie en zijn apetrots met jullie als zonen. Groei uit tot liefhebbende, gezonde mannen. Dat we nog veel mogen spelen, plezier maken, reizen en genieten. Doe wat je graag doet en mama en papa zullen er altijd voor jullie zijn.

Mama, papa en meme, bedankt voor jullie onvoorwaardelijke steun doorheen alles, de goede zorgen voor ons en ook de frequente opvang van de kinderen. Bedankt voor het warme nest, de aanmoediging, kortom bedankt voor alles.

Ook aan heel mijn schoonfamilie; Moeke, Peggy, Tommy, Melissa en Bomma, merci voor de uitjes met de kids, de vele memorabele familiefeestjes. Ik kon altijd zonder zorgen mezelf zijn bij jullie.

Ik kreeg geen kinderen tijdens mijn doctoraat (want die hadden we al), maar ik werd wel meter van 2 lieve schatjes Cien en Julie, mijn 2 prinsesjes. Mijn hart blinkt iedere keer als we samen zijn. Nona is heel trots op jullie en belooft plechtig om met jullie binnenkort vele uitjes en afspraakjes te maken.
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