Summary
Summary

Due to improved medical health care, mortality rate after burns has decreased in the last decades. Patients survive severe burns, but consequently face the morbidity of scarring. For this reason, there is an increasing emphasis on the results of wound healing: the functional and cosmetic scar outcome. The subject of this thesis is the improvement of burn wound healing and scar formation using dermal substitution.

Part I  Cellular and clinical aspects of scar formation

Understanding the different processes of wound healing and scar formation is necessary to improve the outcome of burn patients. Therefore, the first chapters of this thesis review the molecular, cellular and clinical aspects of wound healing and scar formation. Full-thickness burn wounds lead to scar formation, however, in some individuals, the wound healing processes may lead to a hypertrophic scar. Hypertrophic scars are raised, red, inflexible and responsible for serious functional and cosmetic problems. It seems that a wide array of subsequent processes is involved in hypertrophic scar formation, such as the haemostasis, inflammation, reepithelialization, extracellular matrix production and remodeling, neovascularization, and apoptosis. Chapter 2 and 3 focused on hypertrophic scars in particular, as treatment with dermal substitution can improve final scar outcome. In Chapter 2, the complex molecular and cellular key processes that may be responsible for hypertrophic scars were explained and reorganized. It is unclear whether these processes are a cause or a consequence of hypertrophic scar tissue formation, but it is proposed that immunological responses in the beginning of wound healing play an important role. An improved understanding of the processes of wound healing and scar formation may help finding the optimal treatment approach.

In Chapter 3, the current state-of-the-art preventive and curative management of hypertrophic scarring was reviewed. In the prevention of hypertrophic scarring, an optimal treatment of the wound is of importance. In addition, therapies such as silicon, pressure garments and corticosteroids have been described. In the management of existing hypertrophic scars, these therapies have also been applied, along with options such as surgery, laser and cryotherapy. Frequently, the exact mechanism of action of these treatment options is not clarified and treatment effectiveness is generally not investigated in randomized trials. Although hypertrophic scarring commonly occurs following burns, many aspects such as incidence and optimal treatment remain unclear. To investigate the optimal treatment and to evaluate treatment effectiveness, appropriate scar assessment is of eminent importance. Furthermore, recommendations regarding the classification of hypertrophy in the daily practice and in clinical trials are implemented in this chapter.
Part II  Clinimetry: wound and scar evaluation

In the following chapters, several wound and scar evaluation tools were investigated. Both subjective and objective measurements of wound and scar features are indispensable, not only to record the individual progress of healing or scar formation, but also to compare the effect of applied treatments in a research setting. The implementation of evidence-based medicine requires valid and reliable tools for assessment of different wound and scar parameters. Therefore, Chapter 4 and 5 focus on the clinimetric properties of the subjective wound assessment, in particular the wound parameters take of a split-skin graft and rate of epithelialization. In general, these parameters are estimated by the clinician in a bedside procedure; however, this subjective evaluation had not been tested on its clinimetric properties, i.e. reliability and validity. Chapter 4 describes a study in which the reliability of the subjective evaluation of graft take and wound epithelialization was examined. The subjective evaluation of both parameters was found to be reliable if performed by an experienced observer. One experienced observer can obtain adequate reliable results of graft take and epithelialization by means of a single assessment of the wound. Furthermore, experience of the observer was shown to play a role in the reliability of the assessment: experienced observers showed a higher reliability compared to the less-experienced observers.

Besides the analysis of the reliability, the subjective assessment of wound epithelialization was tested for its validity (Chapter 5). In order to determine the validity, the subjective evaluation was correlated with epithelialization measured by digital image analysis. Therefore, reliability of epithelialization measured by digital image analysis was investigated and shown to be good. A strong correlation was found between the subjective evaluation of epithelialization and the measurements performed by digital image analysis, indicating the good validity of the subjective evaluation. Since the measurement with digital image analysis is more time-consuming, the subjective wound assessment seems a valid technique for the daily practice.

In addition to the examination of wound assessment, this thesis also concerns the assessment of the scar. Scar aspects are preferably assessed by both a subjective and objective evaluation, especially in clinical trials. Objective measurement tools for scar characteristics have been developed (e.g. for scar elasticity and color) and are frequently used. Scar surface roughness, which is an important scar aspect for both the patient and the clinician, is often only evaluated subjectively by means of a scar assessment scale. An appropriate, objective measuring instrument for the assessment of scar surface roughness is not yet available in a clinical setting.
Summary

In Chapter 6, the Phaseshift Rapid In Vivo Measurement of the Skin (PRIMOS) (GFMesstechnik GmbH, Teltow, Germany) was tested for its reliability and validity in the measurement of surface roughness of skin and scars. This device noninvasively produces a 3-dimensional image of the skin microtopography and measures surface roughness. The surface roughness parameters of the PRIMOS showed a good reliability for skin and scars: one measurement by one observer was sufficient for a reliable measurement of surface roughness. In addition, results showed a strong correlation between the surface roughness parameter of the PRIMOS and the subjective score for scar roughness. Therefore, this noninvasive measurement tool is a valid and reliable tool for the objective evaluation of surface roughness of both skin and burn scars.

Part III  Clinical application of dermal substitution

In the last chapters of this thesis, dermal substitution was investigated in both reconstructive and acute burn wounds. From 1996 to 1998, our research group performed a clinical controlled trial in which an intraindividual comparison was carried out; in patients with acute and reconstructive wounds, treatment with a dermal substitute in combination with a split-skin graft was compared with treatment with a split-skin graft alone. In this clinical trial, the beneficial effect of dermal substitution was shown in reconstructive wounds. However, in acute burn wounds, no improvement of scar elasticity was seen in the substituted wounds, possibly due to the delayed and reduced graft take in these wounds.

Nowadays, it is generally accepted that dermal substitution can provide a beneficial effect on burn scar outcome. Several studies reported on the positive effects of dermal substitution. Nevertheless, objectively measured long-term data of the effectiveness of this treatment are lacking. Chapter 7 represents the first long-term and objective follow-up of a dermal substitute in which its effectiveness was investigated in acute and reconstructive burn surgery. In this follow-up, several scar aspects of patients treated in the above mentioned clinical trial performed from 1996 to 1998 were measured with subjective and objective evaluation tools. This study showed that reconstructive scars treated with the dermal substitute were significantly smoother compared to non-substituted scars. In addition, scar elasticity was higher in substituted reconstructive scars compared to non-substituted scars, although the difference was not statistically significant. In this long-term follow-up, the long-lasting effect of dermal substitution on scar quality was indicated, mainly in reconstructive wounds.
To improve the effectiveness of dermal substitution in acute burn wounds, it was hypothesized that topical negative pressure (TNP) therapy could increase take rate of the autograft on top of the dermal substitute and consequently improve scar outcome. A four-armed randomized controlled trial was set up to investigate if application of a dermal substitute in combination with TNP therapy could improve scar quality after burns (Chapter 8). Treatment with a split-skin graft with or without the dermal substitute Matriderm®, and with or without TNP were compared in adult patients with deep dermal or full-thickness burns which required skin transplantation. Graft take and wound epithelialization did not reveal significant differences between the four treatment groups. Significantly fewer wounds in the TNP group showed postoperative contamination, compared to other groups. Twelve months postoperatively, highest elasticity was measured in scars treated with the substitute and TNP, which was significantly better compared to scars treated with the substitute alone. This study showed that the use of TNP optimizes the effectiveness of dermal substitution in acute burns.