SUMMARY

A shift in burn care practice has been observed. Advances in acute burn care have significantly placed the mortality of burn injuries in a downward trend. As a result, outcome parameters such as scar quality and quality of life are becoming increasingly important. The studies described in this thesis aimed at improving the outcome of burn patients by concentrating on three domains: burn wound assessment (Part I), scar assessment (Part II), and reconstructive surgery techniques (Part III).

Part I.   Burn wound assessment

Each clinician regularly faces the question 'will this burn wound heal by conservative treatment or is surgical treatment indicated to promote wound closure and thereby perhaps the final scar quality'?

To be able to answer this question, most clinicians will agree that it is essential to perform adequate burn wound assessment, which provides a diagnosis and indirectly also a prognosis. The most frequently used method to assess burn wounds is clinical evaluation, as it is readily available in every country. Using visual and tactile inspection of the surface of the wound, the burn wound can be allocated to a certain category of a classification system. In chapter 2, we described the development of burn wound classification systems over the years and concluded that three classification systems are being used concurrently, resulting in both misunderstanding and the hindrance of correct comparison between clinical studies. We emphasized that it is of great importance to speak a common language both in research and in the clinical assessment of patients with burns, which would be achieved by standardization. Therefore, our proposal is for a versatile scheme, which contains aspects of burn wound pathophysiology, clinical symptoms, a simplified classification system, and designation of treatment modalities. In addition, the scheme comprises outcomes of laser Doppler imaging (LDI), which is currently the best technique based on the state-of-the-art technology as shown in chapter 3. Since it is generally known that it is difficult to assess the exact amount of tissue destruction by clinical evaluation, it is recommended to use LDI to improve the validity of burn wound assessment. The proposed scheme has been developed in such a way that it can be expanded with other measurement tools next to LDI, for example thermography. In chapter 4 and 5, thorough clinimetric evaluations of two thermal imaging tools were performed, to find out whether these measurement tools can assist clinicians in burn wound assessment. Advantages of these tools are their small size, low price and user-friendliness, thereby being examples of low-end technology. It was shown that thermography is pre-eminently feasible, allowing easy and fast measurements in clinical burn practice. Additionally, the technique comprised good reliability, but the validity can be further improved by additional research. Therefore, a larger study is proposed to evaluate the validity of the FLIR ONE thermal imager

when it is used as an add-on test (i.e. clinical evaluation + FLIR ONE versus only clinical evaluation).

By stressing the importance of a uniform burn wound classification system and the use of measurement tools to assist clinicians in burn wound assessment, we intended to encourage researchers and clinicians to pursue standardization in this domain of burn wound care. In addition, it was brought to attention that within burn wound assessment, various constructs can be evaluated. Burn wound depth and healing potential are the most frequently used and closely related, but yet different. Therefore, when performing research, it is essential to provide a precise description of which construct is aimed to measure. In addition, definitions of constructs measuring different aspects of burn wounds should be developed, to better understand the constructs and relationships between these constructs.

Part II.   Aspects of scar assessment

In addition to burn wound assessment, this thesis also concerned various aspects of scar assessment. First, the focus was on assessment of hypertrophic scars and keloids to be able to monitor the response to interventions. Due to the notable thickness of these types of scars, treatment strategies are often directed at flattening of the scar, which in turn makes 'volume' an important scar feature to assess. Until now, there was no tool available to non-invasively measure volume during clinical or scientific follow-up. The study described in chapter 6 showed that three-dimensional (3D) stereophotogrammetry could be used to quantitatively measure scar volume for research purposes. For the clinical follow-up of an individual patient, the measurement error was too high. Currently, other 3D techniques and tools, such as the Structured 3D-scanner™ (Occipital and Lynx laboratories, Boulder, Colorado, USA), are entering the market, which may provide even better results and supreme feasibility. It is anticipated that in the future, 3D techniques will not only be used in scar assessment, but also in reconstructive surgery through 3D scanning and printing of patient-tailored (bioactive) tissue constructs.

In chapter 7, hypertrophic scars were assessed by various techniques (i.e. LDI, colorimetry, subjective assessment and immunohistochemistry) that all focus in a certain way on the aberrant color of these scars. We experienced that the outcome terms of these techniques are used interchangeably, and sometimes gathered under the umbrella term 'vascularization', which can be confusing. Moreover, it was never tested to what extent the outcomes of the techniques are correlated. In our study, only a statistically significant correlation was found between erythema values (colorimetry) and subjective redness assessment (POSAS), which seems to indicate that erythema and redness are associated, but that the other techniques measure different scar features. Therefore, we recommended the use of precise definitions of each outcome in research as well as in clinical practice.

The most experimental study of this thesis was described in chapter 8, in which we investigated the suitability of a custom-made polarization sensitive optical coherence tomography (OCT) system to provide information on scar morphology, in particular, on collagen. OCT is a non-invasive technique, using light to produce images of approximately 1.5 mm tissue in-depth. It was concluded that the birefringent properties of a scar, conceivably constituted by the unidirectional aligned collagen fibers, could be imaged and quantified with the polarization sensitive OCT system. Future work has to be performed to be able to study hypertrophic scars longitudinally in clinical practice, thereby requiring less time for data processing and interpretation.

Part III. New techniques in reconstructive surgery

In the third part of this thesis, new reconstructive surgery techniques for patients with contractures and adherent scars were evaluated, with the aim of improving their quality of life. Due to the considerable limitations in daily life that are caused by scar contractures, surgical treatment (contracture release) is often indicated. In a randomized controlled trial (chapter 9), the effectiveness of perforator-based interposition flaps compared to full thickness skin grafts (FTSGs) was studied for contracture releasing procedures. It was brought to light that perforator-based flaps increase to 142% of the initial surface area over a 12-month period, whereas 92% of the surface area of FTSGs remains. In addition, the final scar quality following a flap procedure was superior compared to FTSGs and we found a lower percentage of necrosis in flaps; 6% versus 17% in FTSGs. Accordingly, it is strongly recommended, if possible, to use perforator-based interposition flaps instead of FTSGs for contracture releasing procedures.

Research at the end of this thesis (chapter 10 and 11) focused on the use of autologous fat grafting (AFG). Severe injuries, such as burns or necrotizing fasciitis, may destruct not only the skin but also the subcutaneous tissue. The resulting scars often become adherent to underlying structures, causing scar stiffness, pain, and sometimes friction and a limited range of motion. AFG provides the possibility to reconstruct a thin but functional sliding layer underneath these scars. We demonstrated sustainable effectiveness of single-treatment AFG, indicated by improved pliability and overall scar quality at 12 months postoperatively. This was the first clinical study assessing the long-term effect of AFG on functional scar parameters using a comprehensive scar evaluation protocol, thereby providing imperative evidence for health insurance companies in the Netherlands. At the moment of finishing this thesis, in June 2017, AFG was reimbursed for this indication.

The current data could be expanded by future research into functional improvement and the patient's mobility after AFG. Especially when several AFG treatments are performed over larger scar surface areas, it would be of interest to investigate the effect on quality of life. In addition to the presented clinical studies on the effectiveness of AFG, a Letter to the Editor was included in chapter 12, in which the results of a randomized controlled trial performed by

colleagues was considered. This appraisal may provide food for thought regarding the set-up of future studies on AFG.

Given the convincing evidence that perforator-based interposition flaps and AFG are effective, versatile and safe, it is recommended that these techniques are added to the armamentarium of reconstructive (burn) surgeons.

In chapter 13, conclusions of this thesis were reviewed and future perspectives were delineated. From the studies described in this thesis, our group has obtained new insights in burn wound classification, outcome measures for burn wounds and scars, the use of terminology, and reconstructive surgery techniques. Finally, upcoming projects such as the development of the POSAS 3.0, big data, and 3D scanning and printing were highlighted, as we feel that these projects will advance burn care in the next years.