Summary
The skin is one of the most important organs of our body, but it is also vulnerable and can easily get damaged. After healing of the damaged skin, scarring is likely to be present. In some cases and in some individuals, abnormal or excessive scarring following damage occurs. Abnormal scarring can cause major physical complaints and aesthetic disfigurement, hence impairing the quality of life of the patient. This thesis describes current scar modalities for the treatment of such abnormal scars. The focus lies on the prevention of hypertrophic scars following acute burn wounds or reconstructive wounds (Part I). In addition, novel keloid scar treatments are evaluated (Part II + III).

Part I. Dermal substitutes for treatment of acute burns and reconstructive wounds

Due to improvements in medical health care, the mortality rate following large burn trauma decreased. However, severe scarring is still seen and therefore new challenges within current burn trauma medicine have risen. Until now, grafting of the burned area with autologous split thickness skin grafts (SSG) is the gold standard. However, severe scarring following grafting with SSG’s is seen. The severe scarring is thought to be due to the lack of dermal tissue in the grafts, which initiated the development of dermal substitutes.

In chapter 2, we outline the biological background of the three main classes of dermal substitutes. Furthermore we relate several characteristics to clinical requirements and discuss the current available dermal substitutes.

In Chapter 3, the clinical implementation of such a dermal substitute is evaluated in a long-term follow-up. This study 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. Seventy-nine percent of the patients of the original study of Van Zuijlen et al, were screened twelve years post-treatment. Both subjective and objective evaluation tools were used. The study shows that even after twelve years, a higher elasticity was seen in reconstructive wounds treated with the dermal substitute compared to the non-substituted reconstructive wounds.
Part II  Intralesional cryotherapy for treatment of keloid scar

Intralesional (IL) cryotherapy is a promising treatment technique in which the scar tissue is frozen from within the lesion. We evaluate IL cryotherapy in a comprehensive review including all clinical studies (chapter 4). Clinically, two different systems were tested in a prospective study; in chapter 5, we evaluate a liquid nitrogen-based system and in chapter 6 we tested an argon gas-based system, which had never been used before for treatment of keloid scars. Compared to the liquid nitrogen system, the argon gas system provided a lower recurrence percentage, but more hypopigmentation post-treatment.

To explain the different outcomes between the liquid nitrogen and the argon gas system, more information about the exact working mechanism of IL cryotherapy was required. Therefore we designed an experimental study, investigating the argon gas and liquid nitrogen system ex vivo and in vivo (chapter 7). In this study the argon gas system showed to reach lower end temperatures and a faster freezing rate compared to the liquid nitrogen system.

Part III  Excision with adjuvant irradiation for treatment of keloid scars

Treatment of keloid scars is difficult with high recurrence rates and even growth stimulus as the main issue. According to the international advisory panel on scar management, surgical excision with post-operative radiation therapy is considered the most efficacious treatment.

In chapter 8, we present a systematic review according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). This review proved brachytherapy to show lower recurrence rates compared to external radiation. Also, a short time (<7hrs) interval between scar excision and irradiation constituted a lower recurrence rate compared to longer time-intervals (>24hrs). Single-fraction irradiation showed promising results in terms of recurrence rate and patient convenience. Finally, scar recurrence was seen between 2 and 36 months, with a mean of 15 months.

In chapter 9, we present our ten years’ experience with a brachytherapy out-patient procedure. The treatment protocol employed a unique radiation schedule with a total dose of 2x6=12 Gray. Importantly, the first dose was administered immediately post-operative and is the lowest dosage known in literature for the treatment of keloids. In a long-term prospective study, we evaluated the effectiveness of this radiation schedule. After 33.6 months we found
a very low recurrence percentage of 3.1%. Also, complaints of pain and pruritus decreased with 82.9% and 87.2% respectively. The unique radiation schedule proved the efficacy and safety of HDR brachytherapy and suggested the importance of immediate postoperative.

Chapter 10 presents a novel method to treat (very) large keloids, which cannot be treated with excision followed with brachytherapy.

Finally, in chapter 11, the most important findings of this thesis and our clinical experience with the devices and are discussed. Lastly, future perspectives are presented in which we direct future research towards the ultimate goal of scar free healing and prevention of even towards prevention of aberrant scar formation.