Perspectives on burn scar evaluation and artificial skin

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Introduction and outline of this thesis

The skin is the largest organ of the human body. It protects the body against fluid loss and defends against invasion of microorganisms. Moreover, it is pliable and able to resist enormous physical stress.

A severe burn injury may interfere with all functions of the skin. In addition, the burn injury frequently has a profound effect on other organ systems such as the circulation, the lungs and the kidneys. Then, a life-threatening situation may develop due to fluid loss, severe bacterial infections, and eventual septic shock. Many patients survive extensive burn wounds nowadays due to advances in resuscitation and antimicrobial therapy. The remarkable reduction of the mortality and morbidity of burned patients increased the necessity and challenge to treat extensive and complicated wounds.

In man, the healed partial or full-thickness wound normally becomes a scar with a poor functional and cosmetic outcome. This is a consequence of the wound healing process that gives a higher priority to the speed of wound healing than to the
quality of the scar. In this way, the occurrence of potentially lethal complications may be prevented. Fast wound closure is obtained by tissue proliferation and wound contraction. Those mechanisms may render the scar hypertrophic and contracted. Although scars start to mature after a few months, functional and cosmetic disturbances frequently remain in the long term. The most dramatic results of scar formation are seen in extensively burned patients. As burn patients with a burned body surface area over eighty percent may survive the burn trauma, scars remain over almost the entire body. Thermal energy may also destroy deeper tissues such as muscles, fat and tendon. The impact of such wounds and scars can be enormous for the patient, especially in regions like the face and hands.

The split thickness autograft has become the mainstay of the treatment of large sized burn wounds. This treatment offers the possibility to resurface large-sized wounds but still leads to scar tissue with poor functional and cosmetic qualities. Moreover, the need for donor sites sometimes exceeds the available unburned skin in extensive burn wounds. The development of artificial skin may circumvent problems that are faced by current burn surgery. The application of artificial skin reduces the need for large donor sites and is hypothesised to serve as a template for wound healing process, allowing a better control of the repair mechanism. The success of culturing keratinocytes to confluent sheets by Rheinwald and Green and the development of an artificial dermis by Yannas and Burke were the first steps towards the development of a tissue engineered skin. The study that led to this thesis initially concentrated on the clinical evaluation of an artificial dermis in acute burn wounds and recon-
Structive surgery at the Burns Centre and the Department of Plastic, Reconstructive and Hand Surgery of the Red Cross Hospital. This dermal substitute was selected after extensive *in vitro* and *in vivo* studies at the Department of Dermatology from the Academic Medical Centre, Amsterdam. A scar evaluation protocol was set up to evaluate the clinical effectiveness of the dermal substitute. This protocol employed an objective and subjective evaluation of the most prominent features of scar formation: colour mismatch, contraction, poor elasticity, and hypertrophy. Biopsies were obtained for evaluation of relevant histologic parameters such as the collagen network architecture. When the protocol was set up we noticed that studies on the reliability and especially the accuracy of scar evaluation tools were sparsely published. How could we rely on these tools when it is unclear what they measure? We therefore reviewed all types of scar assessment tools in the first section of this dissertation and performed two studies to establish the reliability and accuracy of techniques to evaluate vital characteristics of scar evaluation: the contraction of the scar and architecture of the collagen network. The review and both studies are given in chapter 1, 2 and 3 respectively.

Also we noted that long-term outcome of conventional split skin grafting has been sparsely evaluated, maybe simply because the adequate tools for scar evaluation were lacking. Three studies are described in the second section of this dissertation that evaluate the long-term outcome of different aspects of scar formation after conventional split skin grafting. In chapter 4, a long-term functional evaluation is described by objective test criteria, focused on the burned hand. Prognostic factors are identified with respect to the functional outcome. The next chapter, chapter 5, deals with prog-
nostic factors for contraction of the scar, whereas chapter 6 is devoted to a study that quantifies different aspects of collagen structure in scar tissue and in normal tissue.

The last section of this dissertation describes different aspects of the clinical application and development of artificial skin. It starts with a review, chapter 7, on the current status of epidermal, dermal and complete skin substitutes. The clinical effectiveness and microscopic evaluation of a dermal substitute, which is based on collagen and elastin-hydrolysate, is discussed in chapter 8 and 9. This section ends with chapter 10, where an experimental study is described that explores possible fibroblast sources of autologous origin that allow preparation of ‘living’ dermal substitutes. The application of autologous fibroblasts to our acellular dermal substitute has been shown to improve the quality of scar formation in the animal model. At present, a clinical trial is being performed to study the clinical effectiveness of cell seeded dermal substitutes for burn wounds and reconstructive surgery.

References