On burn scar reconstruction

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Summary

During the past decades survival of patients with severe burns has improved significantly. Since more patients survive with a large percentage of total body surface area burned, many more patients now have to deal with the sequelae of scarring: burn scars frequently remain with a poor cosmetic and functional outcome. These burn scar related problems represent a challenge and often require (multiple) reconstructions. To improve the currently available treatment options, research in the field of burn care and burn scar reconstruction is necessary.

This dissertation concerns new developments in reconstructive techniques for problematic burn scars. These presented reconstructive techniques focus on the use of adjacent healthy skin. Because this adjacent healthy skin has unique functional and cosmetic qualities, considering its use instead of other, more technically challenging treatment options can improve the long term outcome after burn scar reconstructions. In the first part of this dissertation we focused on clinimetric research in the field of burn care and burn scar reconstruction. We reviewed the clinimetric requirements of the currently available subjective and objective instruments for measurements of healthy skin and scar tissue (**chapter 2** and **chapter 3**). In addition, two clinimetric studies into the invasive and non-invasive measurements of collagen morphology are presented (**chapter 4** and **chapter 5**). In the second part of this dissertation, we explored and quantified the basic qualities and mechanical properties of healthy skin in comparison with scar tissue, using these clinimetrically tested measurement tools (**chapter 6** and **chapter 7**). The acquired knowledge on basic collagen morphology and the mechanical behavior of healthy skin and scar tissue was translated and applied in the third part of this dissertation where the results of two clinical studies on burn scar reconstruction are presented (**chapter 8, chapter 9,** and **chapter 10**).

I. Clinimetric studies

Scars may lead to an array of cosmetic, psychological and functional problems. Different scar features can be distinguished, i.e. color, thickness, relief, pliability, and surface area, which are clinically relevant and contribute to the quality and judgment of a scar. Reliable and valid measurement of these scar features is nowadays indispensable to practice evidence-based medicine (e.g. evaluate outcome of clinical trials). For measurement of these scar features, subjective and objective scar assessment tools are available. In **chapter 2** the currently available literature on subjective scar assessment scales was reviewed and the currently available scar scales in terms of basic clinimetric requirements were critically discussed. Many scar assessment scales provide reliable

measurements. However, often more than two observers are required to obtain high enough reliability of the results, which limits their feasibility in clinical practice. The validation process of scar assessment scales remains difficult because a “gold standard” is lacking for comparison. Although none of the currently available scar assessment scales met the complete array of basic clinimetric requirements, the most frequently examined and feasible scar assessment scales seemed to be the Vancouver Scar Scale and the Patient and Observer Scar Assessment Scale. **Chapter 3** provided an overview and update on the most relevant non-invasive objective measurement tools for scar evaluation. Based on the scar features color, thickness, relief, pliability, and surface area, the best measurement tools that are currently available were recommended: especially for the scar parameters color, thickness, and relief clinimetric analysis of measurement tools has been performed more extensively and new measurement tools have become available. Nevertheless, the best measurement devices are yet to be determined. Hardly any new measurement tools for pliability and, to a lesser extent, for surface area have been developed recently. For pliability, the Cutometer seems to be the preferred and the most widely used measurement device. For scar surface area, extensive research has already been performed on wounds, thereby providing many suitable measurement methods, ranging from simple transparent acetate measurement to sophisticated camera systems. The ultimate measurement tool of choice for surface area remains dependent on the measurement location and the available budget.

Although in recent years many different objective measurement instruments for healthy skin and scar characteristics have become available, research into measurement tools for collagen orientation and collagen morphometry has been scarcely performed. Since collagen constitutes 85% of the dermis, objective quantification of the collagen organization and collagen morphology is highly relevant to further understand the basic qualities and mechanical properties of healthy skin in comparison with scar tissue. In **chapter 4,** two measurement methods on objective quantification of the collagen morphology were analyzed.

These objective methods, quantifying the collagen bundle thickness and collagen bundle spacing, were tested for their reliability and validity: the Fourier first-order maximum analysis and Distance Mapping, of which Distance Mapping is presented as a newly developed morphometric technique. Both measurement methods were found to be reliable: already one measurement of one observer is sufficient to acquire reliable results. Besides a good reliability of these measurement methods, both Distance Mapping and the Fourier first order maximum had the ability to discriminate between healthy skin and scar tissue, which means that both measurement methods were able to detect a clinically important change. Despite good clinimetric testing of both measurement methods, Distance Mapping was found to be the preferred and most practical measurement method in terms of reliability and usefulness of the outcome parameters. In the future, both methods can be used for reliable and valid collagen morphometry of healthy skin and scar tissue, but also for quantitative microscopic evaluation of other fibrotic processes.

To circumvent the need for a biopsy, which is necessary in the two previously presented measurement methods in **chapter 4**, also possibilities for non-invasive collagen measurements were explored. Therefore, in **chapter 5** clinimetric assessment of a non-invasive measurement tool for anisotropy in healthy skin and scar tissue was presented. Results showed that this measurement tool, the Reviscometer, was a reliable device for anisotropy measurements on healthy skin (on the different locations of the upper arm, forearm and abdomen) and on scar tissue. In addition, clear differences between healthy skin and scar tissue, but also within different locations on healthy skin were identified. Since the Reviscometer was found to be a reliable measurement tool on healthy skin and scar tissue, this non-invasive anisotropy measurement tool has become more eligible to be used in the evaluation of the efficacy of different treatments that aim to improve the quality of scars, diseased skin, and healthy skin. The validity of the Reviscometer should be further investigated.

II. Experimental studies

Using the objective collagen measurement instruments that are presented in **chapter 4**, in the second part of this dissertation basic data were provided on the collagen orientation and collagen structure in healthy skin compared to scar tissue (**chapter 6** and **chapter 7**). In **chapter 6**, a large number of biopsies of healthy skin, normotrophic scar, hypertrophic scar, and keloidal scar tissue was investigated. Objective quantification of the collagen orientation and the collagen structure between healthy skin and scar tissue, but also comparison between different types of scars was performed. It was demonstrated that collagen in scar tissue is organized in a more parallel fashion compared to healthy skin. In addition, it was found that keloidal scar tissue consists of thicker collagen bundles compared to normotrophic and hypertrophic scar tissue. These data further explain basic structural differences between healthy skin and scar tissue and contribute to a further understanding of the pathogenesis of (aberrant) scar formation. In **chapter 7**, the collagen orientation and structure of healthy skin and scar tissue are further interpreted in a dynamic experimental setting. In these ex vivo experiments, cyclical and continuous stretch was applied on strips of healthy skin and scar tissue, thereby mimicking intra-operative skin stretching procedures and splinting therapy for burn scars as applied in clinical practice. Up to now, mechanisms of tissue adaptation in response to stretch were not fully elucidated. Results of this quantitative study objectively showed that stretching of healthy skin and scar tissue induced adaptation in collagen orientation and collagen morphology. Collagen bundles in both healthy skin and scar tissue realigned in a parallel fashion in the direction of stretch and for healthy skin, thicker bundles and more space between the bundles were found. Rapid changes in extension, collagen alignment, and collagen morphology appear to be the underlying mechanism of tissue adaptation in response to stretching. Moreover, it can be concluded that cyclical stretch with lower tension applied should be preferred over continuous stretch with high tension in order to prevent unnecessary tissue damage and to reduce the potential chance on stretch marks. These results can be translated and applied in our clinical studies into burn scar reconstructions which focus on optimal use of the qualities (extensibility) of healthy skin.

III. Clinical studies

In the last chapters of this dissertation, the superior qualities of the adjacent healthy skin were applied in two clinical trials that investigated reconstructive techniques for problematic burn scars. The first prospective study is presented in **chapter 8**, where the adjacent healthy skin was used to improve the current state of the art for burn scar contractures. The applicability of islanded and non-islanded perforator-based interposition flaps as a technique for release of scar contracture was investigated. Patients with burn scar contractures underwent a release using a perforator-based interposition flap. By monitoring the short-term and long-term results, it was found that this concept of perforator-based interposition flaps was a reliable and versatile technique for releasing broad scar contractures. Moreover, it allowed intra-operative tailoring as the flap base can be islanded when indicated. Last, the long-term flap width and surface area measurements demonstrated the superiority of inserting healthy skin into the defect created by the scar contracture release: both the width and the surface area of the flaps had expanded in time, which underlines the sustainability of these perforator-based interposition flaps for scar contracture release.

The results of the second clinical trial are presented in **chapter 9** and **chapter 10.** A multicenter randomized controlled trial was performed to investigate whether stretching the adjacent healthy skin results in excision of a larger burn scar than with conventional treatment. The short-term results as presented in **chapter 9** demonstrated that a significantly larger reduction in burn scar area can be achieved using a skin-stretching device compared to scar excision with no additional techniques. Additionally, no increased risk of complications was reported. It was shown that skin stretching is of added value for large burn scars that cannot be excised in a one-step procedure. Subsequently, in **chapter 10** the sustainability of stretching the adjacent healthy skin was investigated on the long-term. The scar quality up to one year postoperatively was measured, using a large array of reliable and valid measurement tools. Most importantly, these measurements showed the long-term beneficial and sustainable effect of intra-operative skin stretching for wound closure after scar excision: even after one year a significantly smaller scar remained when scars were excised and these wounds were closed with skin stretching. Moreover, it was demonstrated that wounds closed using skin stretching did not lead to wider linear scars or more scar hypertrophy.