A review on porcine burn and scar models and their relevance to humans

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Abstract

Burns are common injuries worldwide and often heal with significant scarring when injury extends into the deep dermal layer. It can lead to hypertrophic scarring, scar contracture, impaired skin function, and disfigurement. Due to the heterogeneous nature of burns and subjective approaches in diagnosis and in outcome, many clinical studies cannot be compared and consensus can be hard to reach. Despite great effort, the mechanism of hypertrophic scarring is still poorly understood, partly due to the lack of animal models with scars similar to human hypertrophic scars. The porcine burn model is widely accepted as the best animal model. This article reviews porcine burn models from the literature and from our laboratory. It details the creation of burns from various methods, the determination of burn depth, the assessment of re-epithelialisation, and the evaluation of the subjective measurements of wound infection and clinical scar outcome. It describes that in our porcine model, burn of 40–50cm^2 with a pale appearance is deep dermal partial thickness, takes more than 3 weeks to completely re-epithelialise and heals with significant scarring that is similar to a human hypertrophic scar. It further draws attention to the relative quantitative approaches of most assessments conducted on our porcine burns/scars and verifies the subjective judgement of wound infection and clinical scar outcome. The information here not only provides essential elements for conducting porcine burn trials, but more importantly offers valuable knowledge for better burn care clinically and for improved clinical trials.

Introduction

Porcine thermal burns have been widely employed for examining the beneficial effects of novel burn treatments prior to clinical application and for understanding the mechanisms of burn wound healing [1, 2]. The advantages of these porcine burns over other animal burns are well described by others, such as the well described close resemblance to human skin in structure and in wound healing. Importantly, unlike heterogeneous burns in humans, the burns created in porcine burn models are relatively consistent in depth, size and location; therefore the effect of manipulations and burn treatment on wound healing outcome can be easily accomplished. Furthermore, in porcine burns the subjective clinical assessment of wound healing and scar appearance can be readily compared with the histological analysis of biopsies, which is usually unavailable in human burns and scars. Nevertheless, many porcine burn models in the literature do not detail all elements described above. It should be noted that Singer and colleagues [1] have thoroughly characterised the burns and scars in their porcine model. This review focuses on these porcine burns/scars from both literature and our own experience and covers the most crucial issues in burns/scars, such as burn depth, wound infection, re-epithelialisation, wound contraction, and scar evaluation, in order to lessen the gap between experimental research and human burns/scars.

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Burn Depth

Clinically, the depth of burns is categorised into first- (superficial), second- (also termed partial thickness) and third-degree burns (full thickness) and determines the choice of burn care and the outcome of burn wounds. Burns with first degree and superficial partial thickness are treated conservatively and heal without scarring, whereas burns

with deep dermal partial and full thickness require skin-grafting and heal with scarring. These scars often require long-term scar management and repeated reconstructive surgery to release contractures. For this reason, well-defined burn depth in a porcine model is demanded. It also provides useful knowledge for the improvement of human burn assessment which is often inaccurately assessed clinically in mid-/deep-partial thickness burns, consequently leading to inappropriate burn care [3, 4].

Many types of porcine thermal burns with different depths, sizes, sharps and locations have been created. Most are contact burns that are created mainly by applying hot brass and aluminium blocks or similar materials [5-15], and also by using hot water in specifically designed devices [9, 16-18]. Some are scald burns by directly exposing skin to hot water [14, 19-21]. While most contact burns are created by hot devices 100°C or less, some are made at higher temperature 150°C–347°C [10, 12, 14, 15]. It should be noticed that creation of contact burns using hot devices is relatively simpler and safer to researchers than the scald burns.

It was established half a century ago that burn depth correlates to heat temperature and duration in pig scald models [22-24]. Since then, the characterisation of burn depth has been further defined histologically where burn depth is determined by: the cell necrosis of hair follicles, mesenchyme and vascular endothelia; damaged collagen; congested blood vessels and thrombosis; extravasation of erythrocytes; and infiltration of neutrophils during the first 3 days post-burn [8, 9, 13, 16]. It is well demonstrated that the extent of injury for different elements in skin tissue is not uniform. The deepest damage occurred in vascular endothelial cells, followed by mesenchymal cells, hair follicles, and collagen, in burns created by an aluminium bar at 50°C–90°C for 10–30s [13]. While superficial burns are relatively stable over time [8, 16], deeper burns can progressively deepen until 24-72 hours post-burn [1, 8]. In contact burns created by a hot device at 170°C, clear demarcations are observed in the dermis: a coagulated superficial layer; injured intermediate layer; and intact deeper dermal layers [9, 14]. In contrast, a mixed pattern of intact and damaged extracellular matrices is seen throughout the dermis and significant damage is only obvious after several days in scald burns with 80°C water [9, 14]. Deep partial thickness burns sized ≥20cm² have been created by applying a brass block 170°C for 20s [10, 14], a contact apparatus 347°C for 5s [15, 25], and by exposing skin to 82-85°C water for 10–12s [19]. Following their important study on porcine burn depth in relation to temperature and duration of exposure [13], Singer et al. uses a aluminium bar 80°C for 20s to create mid-partial thickness burns defined based on the damage in hair follicles and collagen [26, 27].

Since 2004, we have established a porcine burn model in our laboratory [17, 28, 29]. Our burn device is a bottomless Schott Duran bottle covered with plastic wrap at the bottom and filled with 300ml of water. Circular thermal burns sized 40–50 cm² are created by applying this burn device with 92°C water on skin for 15s. The burns are located on the thoracic paravertebral region where the skin surface is flat and large enough to ensure perfect contact with the burn device, and there are either one or two burns on each side. At 92°C for 15s, it is found that the necrosis of hair follicles deepened into the mid-dermal layer, but not in the deeper layer at day 6 post-burn [17]. With this temperature and duration, we have conducted many porcine trials. These trials include: examining the effects of Vitrogro [30], first aid using cool water and others [31-33], and conservative surgical debridement [34] on burn wound healing; and investigating the safety of silver dressing [35, 36].

While clinicians worldwide rely on macroscopic appearance to assess burn depth without histological information; most studies on porcine burns only detail the histological findings but fail to report the corresponding macroscopic appearance of the burns readily at hand. Most of our burns have a uniform "pale" appearance, developed during the burning process, with a rim of erythema around the burn border (Figure 1A, 2A). This "pale" appearance has also been documented on pigs by a few studies [1, 9] and is characteristic of deep dermal burns in humans [3, 4, 37, 38]. Others have reported red burns [16] and burns become redder with shorter exposure [8]. Unlike other studies where the pale burns became red at day 3 post-burn [9] and the rim of erythema subsided within several minutes [1], the pale appearance and the rim of erythema were retained in our burns .

However, some of our porcine burns have a mixed pale and pink (or red) appearance (Figure 1B, 2B), which is noticed in burn photos of other reports [1, 8, 27]. These pink or red areas/burns do not blanch. For pale burns, histological analysis of samples taken immediately after burn injury show necrotic epidermis, completely necrotic hair follicles in the mid-dermis, and necrosis extending even into the deep dermis in some areas (Figure 1A). The capillaries are congested and there is no extravasation of erythrocytes. Two days post-burn, neutrophils are seen between the collagen bundles in the dermis and within the walls of small dermal vessels. For pink burns, histological analysis shows thermal damage to the epidermis and at least partial thermal injury to hair follicles on samples taken immediately after burn injury. However, some of the hair follicles in the middle dermis maintain their structure and are not damaged (Figure 1B). The capillaries in these burns are more dilated and congested in the superficial and mid dermis, with extravasation of

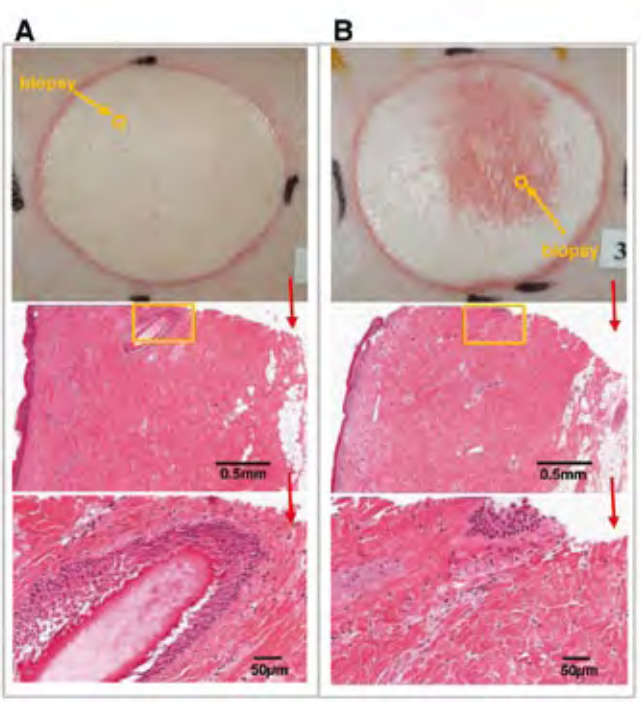

Figure 1. The macroscopic and microscopic appearance of burns immediately after burn injury.

A. *A uniform pale burn. A biopsy was taken from the area indicated by the yellow circle and stained with H&E shown at low and high magnification.* **B**. *A mixed pale and pink burn. A biopsy was taken from the pink area indicated by the yellow circle and stained with H&E shown at low and high magnification.*

red blood cells. During the following two days, there is less inflammation, as indicated by less neutrophils in the dermis, compared to the pale burns. Therefore, burns with a pale appearance are considered to be deep partial thickness burns. The pale burns/areas re-epithelialise slowly and heal with significantly scarring (Figure 2A), whereas the pink burns/areas re-epithelialise quickly and heal with less or no scarring (pink area of burn in Figure 2B) [29, 31]. Only burns with a pale apperance are included in reports where the effect of debridement, anatomic location, different dressings on burn wound healing were evaluated [34, 39, 40].

Re-epithelialisation

In human burns, re-epithelialisation is the major clinical assessment during burn wound healing and a delayed wound healing time is a significant risk factor for hypertrophic scarring [41-45]. Re-epithelialisation is also used to determine the choice of burn care in indeterminate depth burns where these burns receive conservative burn care initially and would only be grafted later if they had not spontaneously healed within 3 weeks. It is commonly assessed subjectively through clinical observation of wounds by experienced burn clinicians.

Re-epithelialisation is also the most common assessment in many porcine burn trials by both macroscopic and microscopic approaches. The non-invasive macroscopic approach, same as in human burns, involves the clinical observation of burns [9, 11, 16, 19] followed by mapping the re-epithelialised areas on a transparent film after gently lifting detachable eschar [46]. However, it is considered to be difficult to assess, mainly due to the thick eschar over the wound [1, 27]. Recently, Singer et al. demonstrated a non-invasive approach, optical coherence tomography (OCT), to reliably assess re-epithelialisation on a porcine excisional model [47]. The invasive macroscopic approach is to macroscopically examine whether the epidermal sheet is defect or intact after excision of wound tissue and separating epidermis from dermis [5, 48, 49]. Microscopic (or histological) assessment of

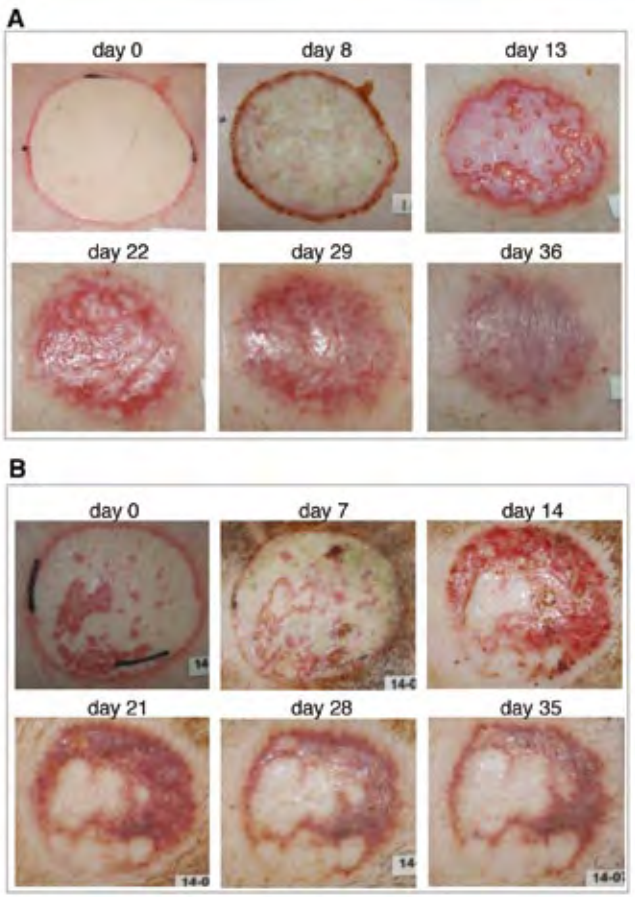

Figure 2. The healing of burn wounds over a 5-week period post-burn

A. *The wound healing of a pale burn and the macroscopic appearance of this burn wound over a 5-week period post-burn.* **B**. *The wound healing of a burn with a mixed pale and pink appearance and the macroscopic appearances of this burn wound over a 5-week period post-burn. Note that the greenish appearances of wounds in some of these photos were caused by cleaning wounds with green-dyed gauze.*

re-epithelialisation is the most common approach and has been used in many studies [9-12, 15, 16, 25, 27].

Most of our porcine trials have a duration of 6 weeks post-burn and re-epithelialisation is assessed at every dressing change either once or twice/week for 6-weeks. Despite being less-accepted compared to histological analysis, the non-invasive macroscopic approach was chosen in our porcine trials. It is conducted by thorough cleaning of wounds, careful examination of wound surface, tracing the re-epithelialised area on Visitrak™ sheets (Smith & Nephew) and then obtaining the absolute value of this area calculated using a Visitrak device. The eschar is softened with saline gauze and then is gently removed without the risk of damage to the wound surface and re-epithelialisation can then be easily judged. Nevertheless, wound photographs must also be taken. On wound photographs, in most cases it is easy to judge re-epithelialisation (day 13 in Figure 2A, Figure 3A), but it can be less certain when mixed re-epithelialised and non-re-epithelialised are doted throughout the wound (Figure 3B&C). The obvious advantage of this approach is that like clinical situations, burn wound healing takes its natural course without the pathological disruption caused by biopsying. Most importantly, this approach is reliable and accurate, allowing one to assess the wound as a whole instead of histological analysis where only biopsying sites and ≈5μm thick sections of these biopsies are examined. This approach is particular useful when burns are relative large. In addition, the information derived from this approach can be easily transferred to clinical situations.

In most of our porcine trials, re-epithelialisation is calculated as % of wound surface for each wound during the 6 weeks post-burn. In burns with a pale appearance, re-epithelialisation only occurs after the first week and usually starts around the border area, with the rest of wound afterward. In a study with 72 burns, it took a mean of 19.8 days (2.8 weeks) to reach 50% re-epithelialisation, and 23.6 days (3.4 weeks) to reach 80% re-epithelialisation [28]. Close analysis reveals that the time to re-epithelialisation is highly correlated to each of the clinical and histological scar assessments. The best correlations of re-epithelialisation are found to be with clinical cosmetic outcomes and histological scar tissue thickness. This demonstrates that our re-epithelialisation data could reliably predict the outcome of burn wound healing clinically and histologically. This further supports the observation in human burn victims that delayed wound healing time is a significant risk factor for hypertrophic scarring [41-45].

Burn Wound Colonisation and Infection

Burn wound infection/sepsis is a serious complication of thermal injury and remains a major threat to human victims

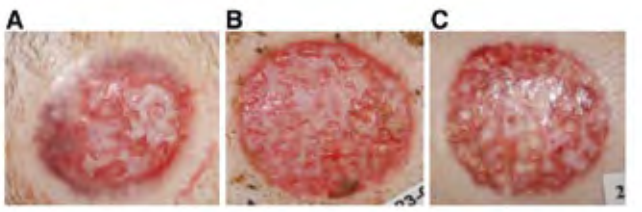

Figure 3. The clinical assessment of burn wound re-epithelialisation on photographs.

The re-epithelialisation can be easily assessed in wound photograph **A** *but is less certain in wound photographs* **B** *&* **C**.

with large burns (>20% TBSA) [50-52]. It is also a main cause for delayed wound healing that leads to a higher risk of hypertrophic scarring. For these two reasons, preventing wound infection remains one of the major focuses in burn care, and regular burn wound inspection by a burn surgeon is mandatory [52]. Burn wound infection is categorised into *wound colonisation*, *wound infection*, *invasive infection*, *cellulitis* and *necrotising infection*. The assessment of wound infection includes both clinical and laboratory examinations. Clinically, the diagnosis of wound infection relies mostly on the clinical symptoms and examination of burn wounds. Quantitative biopsy and swab cultures are considered to be not reliable. Burn tissue histological examination confirms diagnosis but is impractical and rarely used.

Wound colonisation/infection is one of the major assessment categories in our porcine burn trials and is judged by clinical observation of the burn wounds at every dressing change. This includes the amount of exudate, the smell of wound, presence of pus and changes in wound appearance as well as corresponding systemic symptoms. Wound colonisation scores are given from 0-3 where 0 = no colonisation, 1 = mild colonisation with a mild exudate smell and no obvious pus, 2 = medium colonisation with a moderate exudate smell and sign of pus, 3 = severe colonisation with a severe smelling wound and presence of pus and change of colour [53]. In all our porcine burns, only wound colonisation and wound infection are observed. Invasive infection, cellulitis, necrosis and related systemic symptoms are never noted. In our porcine burns, signs of wound colonisation/infection are observed in some as early as week 1, but most by week 2 post-burn when burns begin to re-epithelialise. In a study with 304 porcine burns [53], we found that 19.4% wounds (59/304) were recorded having ≥2 colonization scores at least once over a 6-week period and most of wounds had no sign of wound colonisation. Further evaluation was conducted through Gram staining of 228 burn biopsies, demonstrating that clinical observation of our burn wound infection is consistent with bacterial presence in viable tissue [53]. This result indicates

that in our porcine burns wound colonisation / infection scores are found to significantly correlate with histological scar tissue thickness [39]. The clinical examination of the entire burn wound surface, though subjective, is the most useful and reliable method for diagnosing burn wound infection.

Burn Wound Contraction

Severe scar contracture associated with hypertrophic scarring is often the outcome of wound healing from deep burns, and is the major issue for human burn survivors, particularly for paediatric victims [41, 54, 55]. Currently, the best approach to prevent scar contracture clinically is the early application of pressure garment, but the results are still far from satisfactory. Scar contracture is generally accepted to be contributed by the presence of elevated numbers of myofibroblasts in scar tissue that express α-smooth muscle actin (α-SMA), a factor usually only found in the vessel wall and errector pili muscle in normal skin [55-57]. Myofibroblasts were initially identified in granulation tissue of healing wounds three decades ago [58], and since has been successfully characterised and found to be present in all contracted fibrotic tissue [56, 57, 59, 60].

In both human and animal cutaneous scars, the expression of α-SMA has been extensively investigated. Human scars from paediatric and adult patients were either hypertrophic, non-hypertrophic, or keloid [61-67]. In human burn wounds and scars, myofibroblasts are the dominant cell type in granulation tissue, and α-SMA is more likely to be present or at higher levels in hypertrophic scars than in mature scars and is predominantly localised in the nodular structures and in the more densely populated cell regions in hypertrophic scars [63, 65, 68]. Both pressure therapy and interferon significantly reduce α-SMA expression in human burn scars [63, 65]. In animal models, α-SMA expression has been investigated during wound healing and in scars, with most using small animal excisional models [68-74]. The expression of α-SMA starts during the first week, peaks in the second week and then disappears. In mice and sheep burns, α-SMA expression is found to correlate with burn wound healing outcome [75, 76].

In our porcine burn model, wound size is measured by tracing the wound on a Visitrak sheet at every dressing change and absolute area value is then obtained. The results in most of our reports are scar sizes at week 6 post-burn [28, 34, 39, 40]. In burns with a pale appearance, all scars fail to grow normally during the 6-week period when normal skin expands rapidly to 158% of its original surface area. Most scars became smaller and severely contracted with a mean of 74.5% of the original

burn size in a study with 72 burns [28]. Preliminary multivariate principle components analysis shows that α-SMA expression is highly associated with wound contraction, re-epithelialisation and scar thickness. Higher levels of α-SMA are found in more contracted, thicker scars with delayed wound closure. To our knowledge, this is the first supporting evidence for the association of α-SMA expression with *in vivo* wound contraction, the thickness of scars and re-epithelialisation on large burns, on a porcine model.

Clinical Scar Appearance

Hypertrophic scars in human burn victims present as raised, erythematous, pruritic and inelastic masses of tissue which do not have normal skin architecture/function and are disfiguring [41, 54, 55]. Clinically, to both burn victims and their carers, scar appearance and function are the greatest concerns. Minimal scar tissue and better cosmetic outcomes are the ultimate goals for all burn clinicians and clinical trials of potential new burn treatments, which rely on the proper evaluation of these scars. Clinical evaluation on human scars has been described by many [77-84], and is well correlated with histological scar analyses. This clinical evaluation includes scar vascularity, pigmentation, pliability, height, and surface roughness assessed subjectively and objectively.

In porcine wound healing and scars, though many studies present the photographs of their porcine scars and some provide brief descriptions of these scar appearances, only a few have attempted to systematically rate these scars in the same manner as in human scars. Tennyson et al. [6] employed a visual analogue scale and a clinical assessment scale similar to the human scar scale developed by Beausang et al [77] that includes scar colour, surface shininess, contour, distortion, and texture. Glatter et al [85] used the Vancouver Scar Scale [83], which includes scar pigmentation, vascularity, pliability and height. However, the clinical scar outcome from these two studies on porcine scars was poorly correlated with histological scar outcome.

In our porcine burn scars, a clinical scar scale has been established [28]. It is based on human scar scales [77-84], the difference between human and porcine scars, and the time of assessment (at week 6 post-burn). Most of our porcine burn scars appear severely contracted with red/purple colouration, but are not pigmented. Moreover, scar elevation is usually gradual without sharp elevation at the edges and mostly does not exceed more than 5mm above normal surrounding skin. Our porcine burn scars can then be described as elevated, erythematous, and contracted masses of tissue. Therefore, our clinical scar scale is adjusted to effectively assess our porcine burn scars from best to worst outcome at week 6 post-burn and includes scar height, colour, hair and general cosmetic outcome. Wound contraction is not included in this scale and is obtained quantitatively from wound size. The hair is added in to indicate the preservation of normal skin function, and the scar cosmetic outcome provides a general impression of the scar deviating from normal skin. In this porcine clinical scar scale, the scar is scored between -1– 5 (-1 only for depressed scar height) with normal skin as 0 and the worst scar as 5 [28]. To standardise this assessment and minimize the bias from assessors, a set of porcine scars representing each grade of scar cosmetic outcomes are selected. A set of scar colours from porcine burn scars are also selected as reference colours to represent normal porcine skin colour to dark purple porcine scar colour and this colour bar is also included in the scar photographs to minimize influence of lighting in later experiments. Although requisite scar photographs undoubtedly offer many advantages, the assessment of scars is easier in vivo than on photos, particularly with porcine scar height and hair assessment.

This clinical scar assessment is found to highly correlate with scar histology, wound size, and re-epithelialisation data [28]. More severe scars are clinically characterised by darker purple colouration, more elevation, no presence of hair, histologically by thicker scar tissue, thinner remaining normal dermis, are more likely to have worse contraction, and slower re-epithelialisation. This demonstrates that our clinical scar scale is a reliable and independent tool for assessing porcine burn outcome and truthfully reflects scar appearance/function. Although it is subjective, the scale can be used to assess burn wound healing outcomes without using other healing and scar measuring systems. Of four clinical scar assessments, the scar cosmetic outcome is correlated best with wound healing and scar assessment, indicating that scar cosmetic outcome can substitute for a clinical scar scale in our porcine burn scars when scar colour, height and hair are not available. The "objectivity" of this subjective assessment relies on lessening subjectivity, familiarising with the scar scale, applying reference scars, taking quality scar photos, and placing reference colour bars in scar photos. More importantly, it proves that it is possible to establish a reliable clinical scar scale for porcine burn scars. Undoubtedly, outcomes from the clinical scar scale in porcine trials provide valuable information for subsequent clinical trials.

Histological Scar Assessment

Histologically, hypertrophic scars consist of masses of hypercellular and disorganised connective tissue under a thickened epidermis [41, 54, 55]. Compared to uncomplicated flat scars, their most striking feature is the presence of rounded whorls of immature collagen that range from 0.5mm to more than 1cm in diameter. In a study with human scars,

a histological scar scale focusing on epidermis (related to restoration of rete ridges), the orientation, density and maturity of collagen fibres in the dermis is found to highly correlate to clinical scar scales [77]. Histological analysis has predominated most porcine burn studies, although it is not necessary reported [6, 7, 10, 12, 16, 18, 19, 21, 26, 85, 86]. This includes the inflammatory response, vascularisation, proliferation and maturation of epidermis, granulation tissue formation, dermal remodelling, presence of myofibroblasts, the depth of scarring, the growth of skin appendages, and the immunohistochemical analysis of a variety of molecules involved in wound healing and scar formation. Hoekstra et al. described the thickening of granulation tissue and no viable dermis in some area at days 35-42 following deep dermal burns sized 45cm² inflicted by brass block 170°C for 20s [10]. In full-thickness burns followed by skin grafting, the thickness of granulation tissue was found to peak at day 60 post-grafting, and then decreases over the next 120 days [85]. In order to quantify the severity of burn scarring in a porcine model, Singer et al. designed a histolomorphologic scale incorporating all elements and structures in epidermis and dermis [86]. This scale is very reliable but not highly correlated to clinical scar assessment.

In our porcine trials, scar biopsies are usually collected at week 6 post-burn, and are stained with H&E and some also with Masson trichrome. The histological analysis includes: the thickness of epidermis, organising granulation tissue (early scar tissue layer), and remaining normal-like dermis; the number of hair follicles; and the maturation and appearance of epidermis and dermal collagens. In burns with a pale appearance, scars usually have thicker epidermis and dermis without viable hair follicles. The thicker dermis contains a distinguished thicker layer of organising granulation tissue at the upper portion and a thin layer of normal-like dermis at the deeper portion. This organising granulation tissue is characterised by more basophilic, hypercellular, and finer/not well organised collagen bundles and is often sharply demarcated from the deeper dermis where thicker collagen bundles are arranged in a more orderly fashion similar to that of normal skin. However, round nodules of collagen are not observed in our porcine scars at week 6 post-burn. In a study with 72 burn scars, the quantitative analysis reveals the means of thickness: epidermis = 0.1763mm, organising granulation tissue = 3.534mm, and remaining normal-like dermis = 1.072mm; compared to normal skin epidermis = 0.083mm, and total dermis = 2.2mm [28]. The thicknesses of these three layers, particularly organising granulation tissue, is significantly correlated to clinical scar outcome, wound contraction, and re-epithelialisation. This means that a scar with thicker organising granulation tissue, thicker epidermis and thin remaining normal-like dermis through histological analysis is more likely to heal from delayed wound closure, to appear more contracted, and unfavourable clinical outcomes. Individually, organising granulation tissue could represent histological scar assessment.

In human burn scars, foreign body giant cell reactions are well described and can develop from ruptured epidermal inclusion cysts and residual hair material left behind after the burn injury has destroyed the follicles [54]. In our porcine burn scars, such micro-lesions with characteristics of a foreign reaction to hair shafts are also noticed [87]. Moreover, an additional type of microscopic inflammatory foci is also identified. These microscopic inflammatory foci do not contain any irritant materials, and are composed largely of polymorphonuclear cells with other inflammatory cells including macrophages / epithelioid histiocytes / giant cells, and show acute on chronic inflammatory responses that have not been described previously in burn scars. Importantly, they are present at significantly lower numbers in burns surgically debrided than in burns which have not been debrided. It has not yet been reported how commonly similar lesions occur in human burn scars and how these lesions contribute to the formation of hypertrophic scars. It is currently unpredictable in clinical situations which burns will become hypertrophic, and the pathophysiology of the hypertrophic scaring is not completely understood [88, 89]. It is clear that thorough cleaning/debriding of burned necrotic tissue will minimise the formation of microscopic inflammatory foci in scar tissue.

Conclusion

The essential elements of animal models for any human diseases are the abilities to represent the nature of disease and to properly diagnose and evaluate outcome. This is especially important for burns, since burn injuries possess many variables, such as size, depth and location, and are diagnosed and assessed still through heavy reliance on subjective clinical observation (also not quantitative) rather than laboratory and other specific investigations. Due to these reasons, many clinical and animal burns studies often cannot be adequately compared and cross-interpreted. Moreover, the lack of a suitable animal model with the features of human hypertrophic scars means research suffers greatly. Our porcine burn model reviewed here offers the closest example to human burn scars. Importantly, the depth and location of burns and most crucial aspects of wound healing and scars are well defined and critically evaluated. These burns are relatively large in size with deep partial thickness and heal with significantly scarring histologically and clinically similar to human hypertrophic scars. This model can be used not only for animal trials to promote evidence-based medicine, and provides valuable knowledge to improve subjective

clinical observation and clinical burn care, but also can uncover the mechanisms of hypertrophic scaring.

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