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Experience and outcomes of micrografting for major paediatric burns

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ABSTRACT

Background: The deficit of donor sites in major burns over 50% of the total body surface area has necessitated the application of methods besides traditional meshed autografting to achieve definitive skin cover. The Meek micrografting technique was introduced at this hospital in 2011, especially in the absence of a reliable source of deceased donor allograft skin. The purpose of this study was to evaluate this strategy with reference to its technical execution, efficacy and indications in the context of major paediatric burn surgery.

Methods: A cohort study was performed of all paediatric patients with major burn who underwent Meek micrografting at a dedicated paediatric burn centre in a developing country over a five year period. Demographics, details of their burns, operative management and clinical course and outcomes were collected from patient records and operative notes and analysed.

Results: Thirty-five patients were managed using the micrografting technique during the study period. The mean patient age was 4.1 years (range 3 months–11 years) and their mean total body surface area (TBSA) burn was 49.7% (range 15–86%). Eleven patients sustained inhalation injuries and five developed a re-feeding syndrome on account of delayed referral. The mean abbreviated burn severity index (ABSI) was 8.5 (range 2–13). The hospital length of stay in the 27 survivors was a mean of 75.5 days, equating to 1.4 days per percentage burn. Eight patients died during the course of treatment, with a mean TBSA burn of 67.75% (range 38–86%). Graft take one month after surgery was documented to be more than 90% in 24 patients, of whom 3 subsequently died. Eleven patients had less than 90% graft take at this time, of whom 5 died.

Conclusion: There is a considerable 'learning curve' associated with this technique. In order to achieve success one must ensure a completely viable, non-infected bed, obtained by tangential or fascial excision, followed by allografting as temporary coverage and to 'test the wound bed' for definitive coverage. Infection resulted in the majority of autograft loss in this series, and in addition to risk factors like burn size and inhalation injury, accounted for many of the deaths in this series. Meek micrografting offers high expansion ratios, thereby facilitating durable wound cover in the presence of limited donor sites. It is unlikely that a lethal dose, 50% (LD_{50}) of almost 70% TBSA would have been possible in this context without

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the regular application of this technique. This study advocates for the widespread availability of Meek micrografting and deceased donor allograft skin in developing countries.

1. Background

Rates of survival in major burns in low and middle-income countries (LMIC) are compromised by a deficit of autograft donor skin to obtain definitive wound cover [1]. Standard meshed grafts require the presence of approximately an equal surface area of donor site to cover the excised burn wound. Acknowledging that some sites are inappropriate as donor sites (hands and faces especially) this challenge therefore becomes a critical consideration when the burn wound exceeds forty percent total body surface area (TBSA) [2–4].

To overcome this shortage in available donor skin, the use of alternative methods are required. Deceased donor skin, the availability of which enables prompt complete burn eschar excision to regain physiological equipoise prior to autografting, has been difficult to obtain due to legislative, sociopolitical and cultural challenges, and the absence of a functioning skin bank. The wide expansion of autografts above a ratio of 1:3 (up to 1:9) requires overlay of a skin substitute like Biobrane or allograft to cover the denuded interstices. Cultured epithelial autografts either as spray-on or as sheet grafts are prohibitively expensive, are not readily available, and have considerable functional and aesthetic disadvantages [5].

The modified "Meek" technique of micrografting has offered an alternative form of coverage for extensive areas in the absence of adequate donor sites. This "postage stamp" technique was first introduced in 1958 and modified in 1993. It effectively expands the procured skin surface area between three and nine fold, providing the greatest possible leading skin edges from the geometrically equal epithelial and dermal islands. Modified Meek micrografting is now used globally as a 'rescue method' for definitive coverage for major burn management [6–14].

The "Meek" micrografting system was introduced to South Africa in 2011, specifically to partially compensate for the dire shortage of allograft skin. A retrospective review of patients for whom this procedure was performed was undertaken to define its role in the management of major paediatric burns in LMIC and those without access to a ready supply of allograft [15].

2. Methods

A retrospective study was performed of all paediatric patients with major burn who underwent modified Meek micrografting for definitive skin cover at a dedicated paediatric burn centre over a five year period. Institutional research ethics permission was obtained from the departmental research committee, the University of Cape Town Faculty of Health Sciences Research Ethics Committee and the Provincial Government (HREC REF: 574/2015).

Standard assessment and evidence-based emergency management guidelines were applied as per the Emergency Management of Severe Burns Course, and consensus guidelines of the South African Burn Society [16,17]. Patients were admitted to the paediatric intensive care unit or the paediatric burn centre as required. Demographic characteristics of the patients and their burn were collected, including age, gender, aetiology of injury, extent of burn (%TBSA), proportion of partial and full thickness, and presence of inhalation injury. The number of operations to achieve complete skin cover and methods to achieve skin cover were recorded, as were the wound care strategies undertaken prior to grafting, and the preparations required to optimise graft take (in particular allograft placement). The clinical course of the patients was also recorded, especially with respect to the rate of graft take and proposed or documented reasons for graft loss.

The technique of harvesting, preparation and application of the micrografts are well described using the Meek Micromesher system (Humeca, Netherlands) [4,11]. Thin (0.2–0.3 mm) autografts were harvested, widely expanded micrografts (1:3, 1:4) were prepared and directly transplanted onto the recipient area and covered with a topical stretchable Silver contact dressing (Silverlon®). Following the induction of anaesthesia, completion of the World Health Organisation surgical checklist, the dressings were removed and the burn wounds were washed with 4% chlorhexidine soap followed by the topical application of 0.006% sodium hypochlorite solution for twenty minutes [18]. The initial surgical priority was to reduce the wound surface area as soon as possible to under 30% TBSA. Standard tangential or fascial excision was performed to viable deep dermis, fat or the fascial layer, as necessary. When eschar excision was down to viable fat or deep fascia, the recipient area was pre-conditioned by the application of allograft, when we could obtain this. Deep dermal excisions with a viable bed could immediately be grafted with micrografting. The modified Meek micrografting technique was often used in addition to standard 1:3 mesh grafts with biosynthetic (Biobrane® by Smith and Nephew, UK) or allograft to achieve full skin cover.

The outer dressings were exchanged on day one post-operatively and thereafter on day three and day five. Between day five and day seven the polyamide gauze was removed and the micrografts were covered with an antibacterial bismuth-containing dressing (Xeroform®). These were exchanged on alternate days until full epithelialisation occurred. Occasionally the micrografts were covered with allograft on day seven, if available. One patient underwent cultured epithelial autografting at the time of removal of the Meek micrografts. Vigilant monitoring for infection was undertaken, biopsies were performed when indicated, and bacteria were treated with topical or systemic means, according to the results of culture and sensitivity testing. Where biofilms were suspected, topical Prontosan Gel X was applied empirically with every dressing change. As all of these children came from very

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poor communities with extensive malnutrition, we also recorded co-morbidities prior to the burn that could influence results. These include HIV and Tuberculosis. The refeeding syndrome, consisting of metabolic disturbances of potassium, magnesium, calcium and phosphate, as a results of reinstitution of nutrition in children previously starved or severely malnourished, was particularly difficult to manage.

Rate of graft take is expressed as a percentage and grafted areas were measured in square centimetres (multiplying length and breadth), and derived by consensus of two experienced specialist burn surgeons (more than ten years in practice in a high volume burn centre [more than 1000 admissions per year]). Other data were expressed as the mean with ranges. Statistical analyses were performed as necessary using SPSS software (version 13) with significance set at $p<0.05$. Comparisons were undertaken to assess differences in risk factors between survivors and those who died.

3. Results

Thirty-five patients were treated using the micrografting technique. These procedures accounted for only 3% of burn surgeries undertaken during the study period. The mean patient age was 4.1 years (range 3 months–11 years) and the mean total body surface area (TBSA) was 49.6% (range 15–86%). Twenty-two patients sustained flame burns and 13 scalds; 11 had concomitant inhalation injuries. All patients sustained deep partial thickness to full thickness burns necessitating excision and grafting. Inhalation injury occurred in 11 of the 35 patients. Five of the 35 patients had delayed referrals to the burn centre from outlying hospitals: three of these suffered from the re-feeding syndrome. The mean abbreviated burn severity index (ABSI) [18] for the whole cohort was 8.5 (range 2–13). The mean length of hospital stay in the 27 survivors was 75.5 days (range 10–262 days, 1.4 days/1% burn). Selected patient demographic and surgical details are summarised in Table 1.

A total of eight patients died of their injuries. Their mean TBSA was 67.75%, which was significantly greater than those who survived ($p=0.01$), who had a mean TBSA of 44.18%. The mean age was greater in the deceased group ($p=0.04$), with a mean age of 5.87 in those who died, in comparison with 2.97 years in those who survived. Flame burns were more common in the older group, suggesting deeper burns. Inhalation injury was more common in the group who died ($p=0.001$) with six cases in this group (75%), and 5 in the group who survived (18.5%). Other aetiological factors included multi-organ failure in seven patients and advanced HIV/AIDS in one patient. The re-feeding syndrome, trace element deficiency, kwashiorkor and hypothyroidism, pyroglutamic acidaemia, and ropranolol induced non-occlusive mesenteric ischaemia in the context of sepsis [19] also contributed to the mortality rate. The 27 survivors had a mean ABSI score of 5.9 (range 2–13), while the eight who demised had an average score of 10.1 (range 8–12) [17], a difference that was significant ($p=0.04$).

Deceased donor allograft skin was utilised in 21 patients, either prior to the micrografting procedure, after it, or both (before and after its execution); this is depicted in Tables 2 and 3. In sixteen patients, no allograft was available. Micrografting was performed at a mean time after burn of 28.5 days (range 3–117 days) and a mean area of 29.34% TBSA (range 5–82%) was autografted. The surface area covered with the micrografts was 873.57 cm^2 (range 158.4–3660.8 cm^2). To obtain skin cover, a mean of 7.2 surgical procedures were undertaken (range 1–26), with 2.5 (range 1–26) other surgical

Table 1 – Summary of demographics and surgical details.

	Number (N)	Mean age in years (+−SD)	Mean % TBSA (+−SD)	Mean Meek coverage % TBSA (+−SD)	Mean number of surgeries (+−SD)
Survivors	27	3.47 (+−2.96)	44.19 (+−21)	27.96 (+− 18.73)	6.78 (+− 5.49)
Deceased	8	5.85 (+−2.89)	67.75 (+−17.46)	34 (+−15.68)	8.86 (+− 3.44)
Total	35	4.1 (+−3.08)	49.57 (+−22.37)	29.34 (+− 18)	7.28 (+− 5.13)

Table 2 – Use of Allograft skin with Meek micrografts in surviving patients.

Allograft	Survivors	%TBSA	% Graft take	Comments
Pre-Meek	3	30.5 (15-61)	88.7 (75-100)	Bed preparation
Post-Meek	4	61 (36-86)	77 (20-98)	Onlay graft after sheet removal
Pre- and Post-Meek	6	58 (48-86)	95.1 (85-100)	Bed preparation and onlay graft
No allograft	14	29.8 (15-61)	88.1 (60-100)	Allografts not available

Table 3 – Use and influence of Allograft with Meek micrografts in deceased patients.

Allograft	No. of patients	% TBSA	% Graft take	Comments
Pre	0	0	–	–
Post	1	1	50	Onlay graft over micrografts
Pre and Post	5	5	56.6 (10-90)	Bed preparation and overlay
None	2	2	95 (90-100)	Allografts not available

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procedures preceding the micrografting and a further 2.6 (range 0–10) procedures after micrografting to complete wound cover.

One patient experienced complete graft failure as a result of an extensive *Acinetobacter baumanii* wound infection. Following further wound bed preparation, re-grafting was performed with successful cover obtained. In many cases, when the overlying polyamide gauze dressings were removed after 5–7 days, some detachment of skin islands occurred without significantly impairing the final outcome. In 24 patients (68.5% of the group), graft take on day 14 was satisfactory and, at assessment at one month, was greater than 90%. Three of these successfully grafted patients subsequently died. Eleven patients had less than 90% graft take, with a mean of 56.16% (range 2–80%). Five of these patients died. Wound infections deemed responsible for graft loss included cultures positive for *Pseudomonas aeruginosa* (6), *Klebsiella pneumoniae* (2) and *A. baumanii* (2). The infected wounds were treated with daily sodium hypochlorite 0.006% soaks, followed by Silver sulphadiazine dressings, as determined by wound swab culture results, until the infection resolved.

The 27 surviving patients (TBSA 44.25%) had a mean of 63% of the total wound micrografted. The eight patients who died had 51% TBSA successfully micrografted. The residual areas in both groups were autografted either before or after the micrograft procedures. The length of hospitalisation for the 27 surviving patients, with a mean TBSA of 44.25% (range 15–86%) was 62.2 days (range 7–262), which equates to 1.4 days per percentage burn. Subgroup analysis was performed for those with burns greater than 50% TBSA. The eleven surviving patients within the subgroup had a mean TBSA of 64% (range 50%–86%) in comparison to a mean of 72% (range 52–86%) in the 7 patients who died ($p=0.23$). The lethal dose, fifty % (LD_{50}) within the cohort was calculated to be 67.3% TBSA.

The clinical sequence, from initial presentation to wound closure, of a patient with 48%TBSA flame burn is depicted in Fig. 1.

4. Discussion

The deficiency of adequate donor sites is a limiting factor in achieving wound closure expeditiously in major burns and therefore mandates the use of methods other than standard mesh grafting. The micrografting technique, developed by Meek and adapted by Kreis et al., has become an invaluable tool in the burn surgeon's armamentarium [6,8,20].

Fig. 1 – Meek micrografting process from admission to discharge.

The traditional technique of expanding skin grafts has a mechanical drawback, with significant disparity between expected and actual expansion ratios. The expansion ratio of 1:1.5 has been shown to achieve only 1.23, while for 1:3 ratio, full expansion achieved was only 1.5 using standard dermacarriers [2]. Expansion ratios of 85.5% to 99.8% can be achieved with the Meek technique [3]. Using ratios of 1:3, 1:4, 1:6 and 1:9, a wound surface of 49.2^2–$147.6\,cm^2$ from each original block of $4.2\,cm^2 \times 4.2\,cm^2$ procured donor skin can be obtained [4]. Meek differs from "spray on skin" where non-confluent cells in suspension may not always be correctly orientated (dermal side down) or cultured epithelial sheet grafting which does not expand nor have a dermal component.

This fundamental advantage offered by the Meek system is particularly important when donor sites are at a premium and there is need to cover large surface areas. Autografted islands are in close proximity, are correctly orientated and regularly distributed, rapidly coalescing to cover the interstices by creeping substitution and re-epithelialisation, resulting in a smoother and more uniform clinical appearance [10,11]. This process is usually complete within three weeks, depending on the expansion ratio, the presence of wound infection and the recipient wound bed preparation. The literature describes excellent rates of graft take, ranging from 70–95% [8–12] with the mean graft take in this series was 86.2% (range 2–100%). Wound infection with *A. baumanii* resulted in the most significant case of graft loss.

Meek micrografting should be reserved for specific indications, notably as a rescue procedure to obtain skin closure in the context of major burn when no other strategies are available. Application of Meek micrografting in the context of burns greater than 50% TBSA, is in part responsible for this burn unit's lethal dose, fifty percent (LD_{50}) of 67.3%, a statistic unprecedented in a low and middle income country like South Africa. While unsuitable for face, neck, perineal or hand grafts because the aesthetic and functional results are suboptimal owing to the reliance on secondary intention to complete wound closure, large surface areas can be covered effectively with this strategy in a few operative procedures.

In selected cases Meek micrografting was applied *ab initio*, while in the majority standard 3:1 meshed autografting was undertaken first, and micrografting was used to complement this when donor sites were exhausted. Zermani used mesh grafting to cover 20–35% TBSA (mean 22%) and micrografting to cover the residual 8–10% denuded areas [10], while Hsieh et al. has also used micrografting more selectively, and then only in conjunction with xenografts [12]. Not unlike our experience, Lumenta et al. has used the micrografting technique extensively, and has covered wounds of 61.7% TBSA with a range of 36–80% TBSA [21]. Munasinghe reported an average of 16% TBSA grafted with a 87% graft take, using an expansion ratio of 1:9 [22]. Medina et al. reported their experience with 10 patients with 43%TBSA (10–75%) of wound covered with Meek. Infection was a major problem in all 10 patients, but only on average13% TBSA required regrafting [23].

We have on average, per procedure, covered 25% TBSA (range 5–63%) with micrografts. Other authors have achieved similar results. Lari and Gang covered 16.45% (range 15–20%) in

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Table 4 – Published series on Meek micrografting technique.

Author	N	Age in years	% TBSA	% Meek
Kreis et al. [8]	10	31 (4-52)	64 (43-83) Deep dermal/full thickness: 47(22-71)	10 (5-15)
Raff et al. [9]	41	35.7 (15-81)	54.4 (30.5-80) Deep dermal/full thickness: 50 (30-68)	20-30
Zermani et al. [10]	5	23 (12-51)	36.5 (28-50) Deep dermal/full thickness: 32.6 (20-45)	9 (8-10)
Lari and Gang [11]	7	24 (13-42)	74 (50-85) Deep dermal/full thickness: 56 (33-78)	16.4 (15-20
Hsieh et al. [12]	37	34 (8-80)	72.9 (40-97) Deep dermal/full thickness: 41 (10-90)	13.8 (8-25)
Lumenta et al. [21]	10	46,4 (26-65)	71.6 (60-90) Deep dermal/full thickness: 61.7 (36-80)	61.7 (36-80)
Menon et al. [14]	7	6.1 (2-12)	50 (30-70) Deep dermal/full thickness: 50 (30-70)	Not stated
Munasinge et al. [22]	11	46 (18-77)	56 (20-85) Deep dermal/full thickness: 100	16 (4-36)
Medina et al. [23]	10	35.4 (20-61)	68 (35-90)	43.4 (10-75)
Rode [1]	35	4 (3m-11y)	49.51 (15-86)	31 (5-82)

adolescents and adults [11], Hsieh et al. covered 13.8% (8-25%) of the areas involved [12], Kreis et al. covered 10% (range 5-15%) of the wounds with micrografting in children and adults with 64% TBSA [4,8] and Zermani et al. 29% in both young and older patients [10]. The largest area grafted in one setting in our series was 63% in a 7-year old patient with an eighty percent burn. In an eight month old infant with 13% TBSA we used the micrografting technique, with 1:3 expansion, as a single stand-alone method with excellent outcome. Comparisons with published international literature are tabulated (Table 4).

Adequate excision and temporary closure with allograft has proved to be the single most important recipe for success with micrografting. This almost guarantees a viable wound bed at the time of autografting. Grafting on unstable but viable fat in an immediately excised wound has proved to be largely futile and fascial excision and wound bed preparation with dressings were generally preferred when allograft was unavailable.

Ideally, upon removal of the allograft, "spray on skin" (CEA) would be sprayed onto the newly established wound bed, followed immediately by the overlay of Meek micrografts. We had the opportunity to apply this strategy in one patient, with rapid complete epithelialisation of the entire wound within a week. The use of CEA to enhance epithelialisation at the time of initially applying the micrografts or at the time of sheet removal, should become the norm, wherever possible, and especially in the context of the major burn. We have been reluctant to increase the expansion ratio beyond 1:4 and preferred using 1:3, believing the skin to be more durable during the initial healing process, and less prone to hypertrophic scarring during the rehabilitation phases, especially in our patients, the majority of whom are Fitzpatrick skin types 3 and above. Covering the micrografts is of greater importance if lower expansion ratios are utilised [11].

What became increasingly apparent during our early experience was the need to cover the micrografts on day 7 once the polyamide gauze overlay had been removed, using meshed allografts. Unreliable supply of allograft has compromised our ability to utilise this strategy when required. An alternative to this would have been to use cultured epithelial autograft (CEA) as an adjunctive measure, as reported by Menon et al. [14]. Raff et al. reported an increase in the durability of wound closure with CEA [9]. Epithelialisation was clearly superior when allograft was placed over the autografts after a week, a strategy theorised to offer physical protection to the underlying grafts, prevent desiccation, and the allograft also acts as a scaffold for creeping substitution. Wounds not covered in this way often had areas of overgranulation inhibiting advancing epithelial margins. We generally adopt a conservative approach to this, provided infection was absent, although thicker confluent overgranulation may be carefully scraped away to reveal intact micrografts, allowing epithelialisation to continue. We believe that bio-synthetic dressings applied after polyamide gauze removal should be avoided as the infection risk is potentially too high.

We have been extremely vigilant to address wound infection, and topical antimicrobial dressings have salvaged all cases of infection except for two occasions where extensive graft loss was observed. It would appear that individual epithelial islands can often recover after infection and time should thus be allowed for recovery. Several authors have reported similar experiences [10-12,21-23]. If there were any concerns whatsoever about an infected bed, we perform multiple biopsies for frozen section and undertake immediate bacterial profiling including bio-films, prior to further micrografting. If necessary, the surgery is delayed, preferably using allografts to test the wound bed viability, or we apply a biological dressing or a topical agent to prepare the wound bed.

Although the principle indication for Meek micrografting was as a rescue operation in major burns, six smaller burns were included in the series. The technique was applied in these cases to expedite wound coverage with limited morbidity. The twenty seven patients who survived had a mean TBSA of 44.18% in comparison to the 67.75% in those who died, and all but one of the patients who died had burns greater than 50% TBSA, and five sustained inhalation injuries. In addition, several of the patients in this series had considerable co-morbidities, including HIV, tuberculosis and malnutrition, all

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contributing to delays in obtaining wound cover or independently resulting in their demise.

Unfortunately, we are unable to comment on the long term aesthetic outcome of many of the patients, as many are resident in distant low-income informal settlements, and follow-up is extremely challenging. The majority of cases were followed-up for at least a year. In five cases, we have documented good to excellent aesthetic and functional outcomes for 5 years. Some of these had both standard 1:3 meshed grafts and 1:3 micrografts; the micrograft outcomes were at least equal but often superior to those of the meshed grafts (Figs. 2 and 3). A separate prospective study is underway to assess the cosmetic sequelae of patients who undergo micrografting, which is especially relevant given the propensity for hypertrophic scarring and keloid formation in our patient population. Several authors, however, have reported on the favourable functional and aesthetic outcomes of micrografting, with the surface areas uniformly smoother, softer,

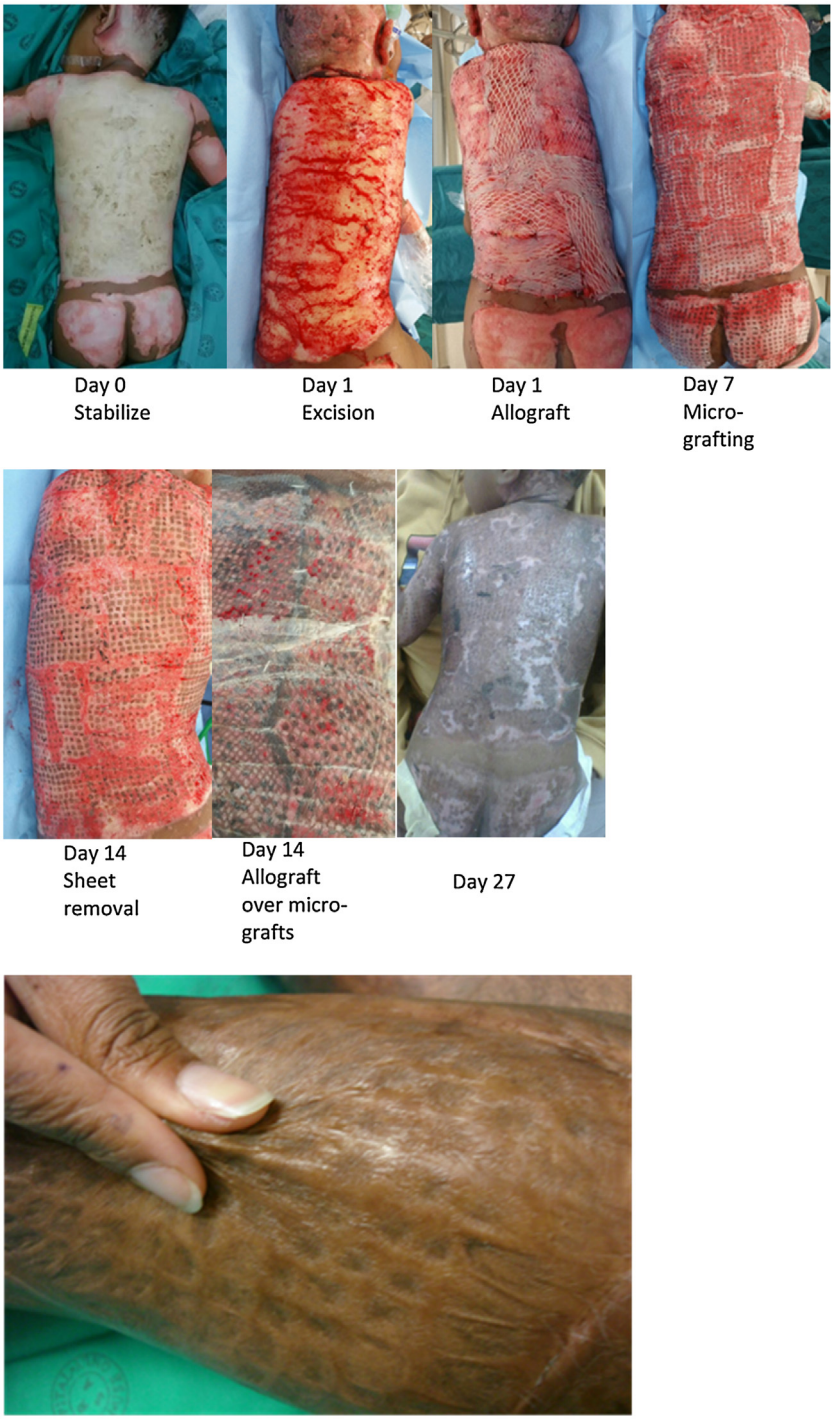

Fig. 2 – Suppleness of micrografts.

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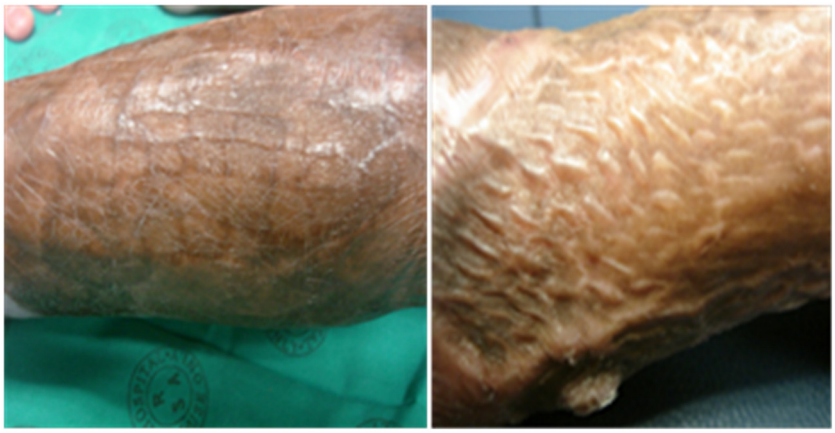

Fig. 3 – Comparison of meshed grafts (1:1,5) and micrografts (1:3) in the same patient.

and more pliable than standard widely expanded grafts [8,12,22].

5. Conclusion

The micrografting technique is ideally suited to application in the context of major burns requiring skin cover in the presence of limited donor areas. Large expansion ratios are possible, graft take and epithelialisation is satisfactory and the cosmetic appearance is comparable to standard widely meshed grafts. Meticulous attention to adequate debridement and wound bed preparation, preferably with the use of donor deceased allograft, as well as the vigilant prevention and management of infection, is critical to successful outcomes. The LD_{50} of 67.3% TBSA in this study is acceptable taking into account the adverse co-morbidities of the study population.

Conflict of interest

The authors declare that there was no conflict of interest nor financial gain related to this study.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.burns.2017.02.008.

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