Original Article

Long-Term Clinical and Histological Evaluation of PoreSkin: A Human Acellular Dermal Matrix in Burn Scars, a Descriptive Clinical Study

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Background: PoreSkin, a first and only human acellular dermal matrix [hADM] developed in Thailand, has been reported to have a satisfactory engraftment rate without any signs of rejection or any other complications in the treatment of burn scars. Although a previous study had demonstrated the favorable short-term clinical results, the long-term clinical, and histological results should be evaluated.

Objective: To assess the long-term clinical and histological results in burn scars treated with PoreSkin for more than 18 months.

Materials and Methods: Ten patients with burn scar deformities had been treated with PoreSkin placement and subsequent delayed thin split-thickness skin grafting for more than 18 months were enrolled in the present study. Percentage of scar contraction was measured using the standard graph paper technique. Vancouver scar scale was used to evaluate the improvement of the scar quality. Punch biopsy specimens from the grafted area were taken for light and electron microscopic examination.

Results: After 18 months, the mean contraction percentage of the area treated with PoreSkin and subsequent delayed thin split-thickness skin grafting is 44.6% (22.8% to 55.9%). Scar quality is significantly improved according to Vancouver scar scale. Histological finding showed no inflammatory cells, normal capillary formation, increased fibroblast, and collagen proliferation; however, most of them were in disorganized pattern.

Conclusion: The long-term result of PoreSkin reconstruction as a dermal substitute showed significant improvements in grafted area scar quality. Substantial area of contraction had occurred. Normal capillary formation was identified. Increased fibroblast and collagen proliferation although in disorganized arrangement were presented in all specimens. No inflammatory cell was found.

Keywords: Burns, Acellular dermal matrix, Acellular dermal regeneration template, Dermal substitute, Wound healing

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Acellular dermal regeneration template has been increasingly a more viable alternative for skin replacement. Their favorable outcomes are considered beneficial for chronic ulcers, as well as for acute wounds and reconstructive surgery. Acellular dermal matrix was showed to have a beneficial effect on wound healing in both animal and human studies[1,2]. In several clinical studies, the use of dermal matrix had demonstrated faster dermal maturation, better scar quality, and a tendency to reduce wound contraction[1-4]. Anyway, few long-term unfavorable results such as shrinkage, partial depigmentation, and hypertrophic scar had also been reported.

PoreSkin is the first and only human acellular dermal matrix [hADM] developed in Thailand. PoreSkin, a bilayer hADM is a porous wet-sponge collagen with a thin sheet of semi-permeable silicone membrane coverage. The collagen is made from an extraction of human cadaveric dermis. The lyophilized dermal extract solution is fabricated into 2 mm thick membrane. The membrane is a highly interconnected porous structure with an average pore size of 150±29 µm. The use of this dermal regeneration template had shown favorable clinical outcomes without any complications in the treatment of burn scars[5]. The present study was designed to evaluate the long-term clinical appearance of PoreSkin in terms of shrinkage and quality of scar as well as its histological features.

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Materials and Methods

A descriptive clinical study was conducted between November 2010 and April 2013. Ten patients had burn scar revision using PoreSkin and thin split-thickness skin graft 18 months earlier were enrolled in the present study. The study was approved by the Institutional Review Board of the Faculty of Medicine at King Chulalongkorn Memorial Hospital, Bangkok, Thailand. All patients underwent two-stage traditional dermal template and skin graft reconstruction. The second stage was done at 21 days using an 8 in 1,000 inches autograft harvested with Zimmer® dermatome. The area of treated scar was evaluated by computer software (Image J, 1.42q/Java1.6.0.10).

Baseline clinical data including the quality of the scar using the Vancouver scar scale were collected prior to surgery. After a thin autograft was placed on the neodermis, the whole resurfacing area was mapped using standard scale plastic sheet. Apart from other clinical evaluation measurement, mapping of each resurfacing area by adopting the same technique was performed at two weeks, one month, three months, six months, twelve months, and eighteen months. After eighteen months, the quality of each scar was assessed using the Vancouver scar scale[6,7].

A punch biopsy was done on each resurfacing grafted area for histological study. The specimens were examined using light and electron microscopy by an appointed histopathologist expertise in skin and soft tissue.

Study endpoints

The primary outcome measure was the percentage of scar contraction after eighteen months of PoreSkin and the skin graft resurfacing. Quantitative scale using the standard scale plastic sheet was used to calculate the percentage of contraction[8]. The secondary outcome measures were histological findings after eighteen months, and the final cosmetic result.

Statistical analysis

The results were expressed as mean ± SD. All statistical analyses were performed by the SPSS version 23.0. A one-way repeated measure ANOVA was conducted to compare the effect of time after operation (independent variable) on wound area (dependent variable), percentage of wound area and percentage of wound contraction at day 0, two weeks, one, three, six, twelve, and eighteen months. Pair t-test analysis was conducted for difference in the Vancouver scar scale pre- and post-operatively[5,6]. A p-value of less than 0.05 was considered significant.

Results

Ten patients attended the follow-up clinic at the appointed periods up to 18 months after they underwent traditional PoreSkin dermal template and subsequent thin split-thickness skin graft reconstruction. Demographic data and the reconstructed anatomical sites are shown in Table 1. To determine the percentage of contraction of PoreSkin with thin split-thickness skin graft after 18 months, each resurfacing area was calculated in square millimeter and percentage at every follow-up period as showed in Table 2 and 3. Percentage of shrinkage or contraction was then calculated based on these data (Table 4). Despite the improved result of the scar after surgery, the resurfacing area gradually contracted up to 18 months. The study has shown that the average mean percentage of PoreSkin and subsequent thin split-thickness skin graft contraction is 44.6% after 18 months (22.8% to 55.9%).

The quality of the resurfacing area of each scar was improved in all components according to the Vancouver scar scale. Pigmentation and pliability was the most improved two components. The quality of the scar after 18 months was better with statistically significant difference in the Vancouver scar scale (p = 0.001) (Table 5).

Histologic examination

Histology of the full-thickness biopsy specimens taken from the grafted area showed partial reconstituted rete ridges of epidermis in all specimens. There were no inflammatory cells or foreign body giant cells in all specimens. Normal capillary formation was identified in most of the specimens. Increased fibroblast and

Table 1. Demographic data

Data	Total case (%)
Age (years), mean (range)	32.4 (18 to 50)
Sex	
Male	6 (60)
Female	4 (40)
Cause	
Scald	6 (60)
Flame	2 (20)
Chemical	2 (20)
Burn percentage (%), mean ± SD (range)	19.2±10.5 (5 to 42)
Study site	
Chest	3 (30)
Upper arm	2 (20)
Forearm	4 (40)
Hand	1 (10)

Table 2. Grafted area during follow-up

Study site number	Wound area (mm^2)						
	Day 0	2 weeks	1 month	3 months	6 months	12 months	18 months
1	3,963	3,836	3,547	2,743	2,127	1,808	1,782
2	1,341	1,245	1,148	908	875	823	796
3	3,053	2,775	2,314	1,770	1,738	1,683	1,478
4	1,989	1,884	1,655	1,334	1,162	1,024	941
5*	7,525	7,488	7,212	6,811	6,303	6,102	5,807
6	2,772	2,391	2,010	1,769	1,656	1,516	1,483
7	5,231	4,886	4,405	3,745	3,374	3,243	2,897
8	6,471	5,662	4,866	4,109	3,940	3,881	3,821
9	1,347	1,201	1,029	819	704	649	594
10*	2,770	2,502	2,470	2,012	1,925	1,801	1,784
Mean*	3,646	3,387	3,066	2,602	2,380	2,253	2,138
SD	2,130.9	2,060.7	1,952.4	1,847.0	1,718.4	1,694.6	1,619.5

* $p = 0.029$, decrease in size of the grafted area by time after surgery

Table 3. Percentage (%) of grafted area during follow-up

Study site number	Percentage of wound area (%)						
	Day 0	2 weeks	1 month	3 months	6 months	12 months	18 months
1	100	96.8	89.5	69.2	53.7	45.6	44.9
2	100	92.8	85.6	67.7	65.2	61.4	59.4
3	100	90.9	75.8	58.0	56.9	55.1	48.4
4	100	94.7	83.2	67.1	58.4	51.5	47.3
5*	100	99.5	95.8	90.5	83.8	81.1	77.2
6	100	86.3	72.5	63.8	59.7	54.7	53.5
7	100	93.4	84.2	71.6	64.5	61.9	55.4
8	100	87.5	75.2	63.5	60.9	59.9	59.0
9	100	89.2	76.4	60.8	52.3	48.2	44.1
10*	100	90.3	89.2	72.6	69.5	65.0	64.4
Mean*	100	92.0	83.0	68.0	62.0	58.0	55.0
SD	0.0	4.1	7.6	9.0	9.2	10.1	10.2

* $p = 0.006$, decrease in percentage of the grafted area by time after surgery

Table 4. Percentage (%) of grafted area contraction

Study site number	Percentage of wound contraction (%)						
	Day 0	2 weeks	1 month	3 months	6 months	12 months	18 months
1	0	3.2	10.5	30.8	46.3	54.4	55.1
2	0	7.2	14.4	32.3	34.8	38.6	40.6
3	0	9.1	24.2	42	43.1	44.9	51.6
4	0	5.3	16.8	32.9	41.6	48.5	52.7
5*	0	0.5	4.2	9.5	16.2	18.9	22.8
6	0	13.7	27.5	36.2	40.3	45.3	46.5
7	0	6.6	15.8	28.4	35.5	38.1	44.6
8	0	12.5	24.8	36.5	39.1	40.1	41
9	0	10.8	23.6	39.2	47.7	51.8	55.9
10*	0	9.7	10.8	27.4	30.5	35	35.6
Mean*	0	7.9	17.3	31.5	37.5	41.5	44.6
SD	0	4.1	7.6	9	9.1	10.1	10.2

* $p = 0.006$, increase in percentage of the grafted area contraction by time after surgery

Table 5. Vancouver scar scale [VSS]

Study site number	Vancouver scar score		Difference
	Pre-operative	Post-operative (18 months)	
1	11	6	5
2	9	5	4
3	9	5	4
4	10	4	6
5	10	5	5
6	8	4	4
7	6	2	4
8	11	6	5
9	8	4	4
10*	9	5	4
Mean ± SD			4.5±0.7

* There was a significant difference in pre-operative VSS (mean 9.1, SD 1.52) and post-operative VSS (mean 4.6, SD 1.17), t (9) = 20.13, $p = 0.001$

collagen proliferation were found in dermis in all specimens; however, most of the collagen fiber orientation was in disorganized pattern. Scanning electron microscope [SEM] examination showed thickening of the collagen fiber in dermal layer (Figure 1).

Discussion

There are two stages of skin graft contraction. When the skin is harvested from the donor site, it undergoes immediate reduction in size, which is called primary contraction. It occurs more in full-thickness skin graft than split-thickness skin graft. When a skin graft is placed on its recipient site, it then undergoes secondary contraction. This contraction reduces the size of the graft along with its interface with the recipient bed and the whole circumference of the graft. It is the graft thickness that determines the degree of contraction. In the case of secondary contraction, it is the split-thickness grafts that contract more than the full-thickness grafts[9].

The amount of dermis in autologous skin grafts crucially determines the overall quality of the grafted wound and the degree of contraction. The tendency of split-thickness grafts to contract more is due to its limited content of dermal tissue. The acellular components in the dermis are considered to play a major role in influencing graft outcomes[10].

There is a need for an effective dermal replacement since dermal tissue does not regenerate into normal dermis after full-thickness dermal injuries. Without the adequate dermal matrix, the formation of scar tissue is followed. Scars, in many circumstances, cause both esthetical and functional problems due to their contracture[11].

Since the degree of scarring and contracture of a full-thickness wound correlate inversely to the amount of dermis implanted to the wound[12], if split-thickness skin graft had to be used instead of full-thickness skin graft for any circumstance, the dermal matrix should be replaced. Theoretically, the two-stage dermal template and split-thickness skin graft reconstruction should be the procedure that could achieve the comparable result to the full-thickness skin graft. The secondary contraction of the full-thickness skin graft had been reported to be between 33% and 48% depending on the anatomical sites and infection[13].

There were many reports on the use of such composite skin grafting. However, most of them were limited by small grafted areas and short clinical follow-up. In the present study, despite the improved result of the scar after surgery, the resurfacing area gradually contracted up to 18 months. The study had shown that the average mean percentage of PoreSkin and subsequent thin split-thickness skin graft contraction was 44.6% after 18 months (22.8% to 55.9%). There was no acute or chronic rejection observed in the present study during the long-term period of follow-up which was similar to the result of most previous studies[14-18].

Long-term histological examination of previously reported acellular dermal matrix reconstruction had shown vary results from normal collagen to increased collagen of variable arrangement[14]. In the present study, increased fibroblast and collagen proliferation were found in dermis in all specimens, however, most

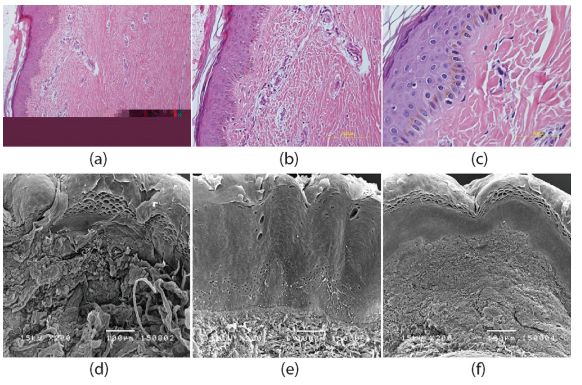

Figure 1. Histological study of PoreSkin under light and electron microscope after 18 months comparing with the normal skin and previously excised scar: (a) PoreSkin (x10), (b) PoreSkin (x20), (c) PoreSkin (x30), (d) Normal skin (x200), (e) Scar (x200), (f) PoreSkin (x200).

of the collagen fiber orientation was in disorganized pattern. SEM examination showed thickening of the collagen fiber in dermal layer (Figure 1).

Conclusion

PoreSkin, a hADM reconstruction after 18 months showed significant improvement in grafted area scar quality. The average mean percentage of grafted area contraction is 44.6% after 18 months (22.8% to 55.9%). There were no inflammatory cells and foreign body giant cells in all specimens. Normal capillary formation was identified in most of the specimens. Increased fibroblast and collagen proliferation were found in dermis in all specimens; however, most of the collagen fiber orientation was in disorganized pattern with thickening of the collagen band.

What is already known on this topic?

PoreSkin, a first and only human dermal matrix developed in Thailand, has been proven to have a satisfactory engraftment rate without any signs of rejection or any other complications.

What this study adds?

The long-term result of PoreSkin reconstruction as a dermal substitute showed significant improvements in scar quality. Considerable area of contraction had occurred. No inflammatory cell was found. Normal capillary formation was identified. Increased fibroblast and collagen proliferation were found although in disorganized arrangement.

Potential conflicts of interest

The authors declare no conflict of interest.

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