Initial Experience With Autologous Skin Cell Suspension for Treatment of Deep Partial-Thickness Facial Burns

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Facial burns present a challenge in burn care, as hypertrophic scarring and dyspigmentation can interfere with patients' personal identities, ocular and oral functional outcomes, and have long-term deleterious effects. The purpose of this study is to evaluate our initial experience with non-cultured, autologous skin cell suspension (ASCS) for the treatment of deep partial-thickness (DPT) facial burns. Patients were enrolled at a single burn center during a multicenter, prospective, single-arm, observational study involving the compassionate use of ASCS for the treatment of large total BSA (TBSA) burns. Treatment decisions concerning facial burns were made by the senior author. Facial burns were initially excised and treated with allograft. The timing of ASCS application was influenced by an individual's clinical status; however, all patients were treated within 30 days of injury. Outcomes included subjective cosmetic parameters and the number of reoperations within 3 months. Five patients (4 males, 1 female) were treated with ASCS for DPT facial burns. Age ranged from 2.1 to 40.7 years (mean 18.2 ± 17.3 years). Average follow-up was 231.2 ± 173.1 days (range 63–424 days). Two patients required reoperation for partial graft loss within 3 months in areas of full-thickness injury. There were no major complications and one superficial hematoma. Healing and cosmetic outcomes were equivalent to, and sometimes substantially better than, outcomes typical of split-thickness autografting. Non-cultured, ASCS was successfully used to treat DPT facial burns containing confluent dermis with remarkable cosmetic outcomes. Treatment of DPT burns with ASCS may be an alternative to current treatments, particularly in patients prone to dyspigmentation, scarring sequelae, and with limited donor sites.

Deep partial-thickness (DPT) facial burns pose a significant challenge to the burn surgeon. Current burn treatment consists of excision and subsequent application of split-thickness skin graft (STSG), which may result in dyspigmentation and hypertrophic scarring at the seams, borders, and within the grafts. This is particularly problematic in patients with facial burn injuries, due to the greater associated psychosocial issues than typically observed for comparable burn injuries in other areas of the body.[1] Scarring can further contribute to oral and ocular impairment and dysfunction, potentially requiring complicated reconstruction. A technique to improve the outcomes of DPT facial burns is needed.

Wood et al have reported the use of a point-of-care device to prepare an autologous skin cell suspension (ASCS) that is used for the treatment of acute burns (RECELL®, AVITA Medical, Valencia, CA).[2, 3] The resulting suspension contains keratinocytes, fibroblasts, melanocytes, and Langerhans cells.[4] When the suspension is applied to DPT burns, decreased rates of dyspigmentation and hypertrophic scarring, decreased donor site morbidity, decreased postoperative pain, and comparable healing rates have been observed when compared with conventional STSG.[5, 6]

The ASCS device has undergone evaluation within two multicenter, prospective, randomized, controlled trials in the United States.[5, 7] In these trials, the face was excluded from evaluation. Within this study, we report results of the treatment of DPT burns of the face using ASCS as part of a concurrent compassionate use protocol.

METHODS

Study Design

This study is a retrospective cohort analysis of subjects with DPT facial burns treated under an Institutional Review Board approved compassionate use protocol (FDA IDE 15945, NCT02992249) utilizing the RECELL® System (Avita Medical). Patients with life-threatening injuries who lacked adequate skin to harvest for conventional skin grafting were eligible for enrollment. For this study, this was classified as an injury greater than 30% total BSA (TBSA). Additionally, the treating investigator had to determine that the risk associated with the use of ASCS was no greater than the probable risk from the burn injury and that the patient had the potential to realize benefits from the application of ASCS. Patients were disqualified if they had an active infection or a known hypersensitivity to trypsin or compound sodium lactate (Hartmann's) solution. Informed consent/assent was obtained prior to surgical intervention.

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Treatment

Patients presented to the hospital for emergency admission secondary to burn injury. Time from presentation to the first procedure for treatment of the facial burn varied as part of a comprehensive burn care plan for the patient's extensive injuries. Patients identified as having DPT facial burns were treated with initial tangential excision and allograft placement followed by ASCS to all unhealed areas. Excision was performed with sharp instrumentation, and some combination of Weck blade and Versajet® hydrosurgery system was implemented for all burns. Hemostasis was achieved with epinephrine-soaked Telfa gauze and Bovie electrocautery, as clinically indicated.

Preparation of ASCS

ASCS was prepared per the manufacturer's recommendations and protocol. A skin sample (0.006–0.008 inches thick) was harvested from an intact area with a Zimmer® dermatome (Zimmer, Indiana). When possible, the thigh was used as a donor site, but the torso (including abdomen, chest, and back) was also used in four patients (80%). This sample was cut into 6 cm^2 samples that were transferred to a proprietary enzyme formulation for 15 to 20 minutes to breakdown adhesions between cells and the extracellular matrix, including those found at the dermoepidermal junction. Following enzymatic incubation, the sample was rinsed with a buffer solution and mechanically scraped with a scalpel to disaggregate cells from the dermoepidermal junction. The resulting cells were suspended in a buffer solution, filtered, and drawn into the treatment syringe for application to the excised and hemostatic burn wound bed.

Postoperative Dressing Management

Once the ASCS was applied to the treatment areas of the face, the wounds were dressed with Telfa clear dressings, followed by a secondary dressing of Xeroform™ Occlusive Petrolatum Gauze Dressing (Covidien), which acts to mold the Telfa clear to the face. The Xeroform was changed on postoperative days 2 and 4 while the Telfa clear was left in place. On postoperative day 7, all dressings were taken down and treatment sites were evaluated by the senior authors (J.A.M., J.E.C., and J.H.H.).

Study Endpoints

Per protocol, healing was defined as the presence of ≥95% reepithelialization with an uninterrupted layer of viable epithelium. Secondary outcomes included subjective cosmetic parameters, postoperative complications, and number of reoperations within 3 months after application of ASCS. To document outcomes, appropriate consent/assent was additionally obtained for photographs in compliance with our institutional standard and the protocol requirements.

STATISTICAL ANALYSIS

Data analyses were performed using the Statistical Package for the Social Sciences Windows version 13.0 (SPSS, Chicago, Illinois). Descriptive statistics for continuous variables were the mean and standard deviation, after confirmation of normal distribution.

RESULTS

From June 2016 to May 2017, 26 patients were treated for large TBSA burns under the compassionate use protocol for ASCS at our institution. All patients sustained greater than 30% TBSA thermal injuries. Of these treated patients, 5 received ASCS treatment for DPT burns of the face. All burns were thermal, resulting from a flash/flame mechanism. The mean time from burn injury to initial excision and allograft placement was 5.6 ± 2.1 days, with a range of 4 to 9 days. Mean time from initial burn to application of ASCS was 20.6 ± 6.5 days, with a range of 12 to 29 days (Table 1).

Age ranged from 2.1 to 40.7 years at the time of first operation, with the mean age being 18.2 ± 17.3 years. Of the five patients, four were male and one was female. Average follow-up duration was 231.2 ± 173.1 days, with a range of 63 to 424 days. No patients experienced complete graft loss or infection postoperatively.

Reoperation within 3 months of initial surgery occurred in two of the five patients, due to partial graft loss in areas that were full-thickness injuries. One patient experienced a superficial hematoma that resolved without surgical intervention. Photographs of patients at the time of ASCS application and at routine interval follow-ups are shown in Figures 1–5.

DISCUSSION

Treatment strategies for burn wounds are largely dependent upon the depth of injury. Superficial partial-thickness burns will heal with a variety of topical treatments. Full-thickness

Table 1. Subjects and treatment details

Subject	Age (years) / Sex	% TBSA	Time From Injury to ASCS (days)	Location of Donor Site
1	33/M	52	21	Bilateral lower extremities
2	4/M	49	12	Back, abdomen, buttocks, and bilateral thigh
3	2/M	35	29	Back, buttocks
4	40/M	52	24	Back, bilateral thighs
5	12/F	62	17	Anterior/posterior torso

%TBSA, percent total body surface area burned.

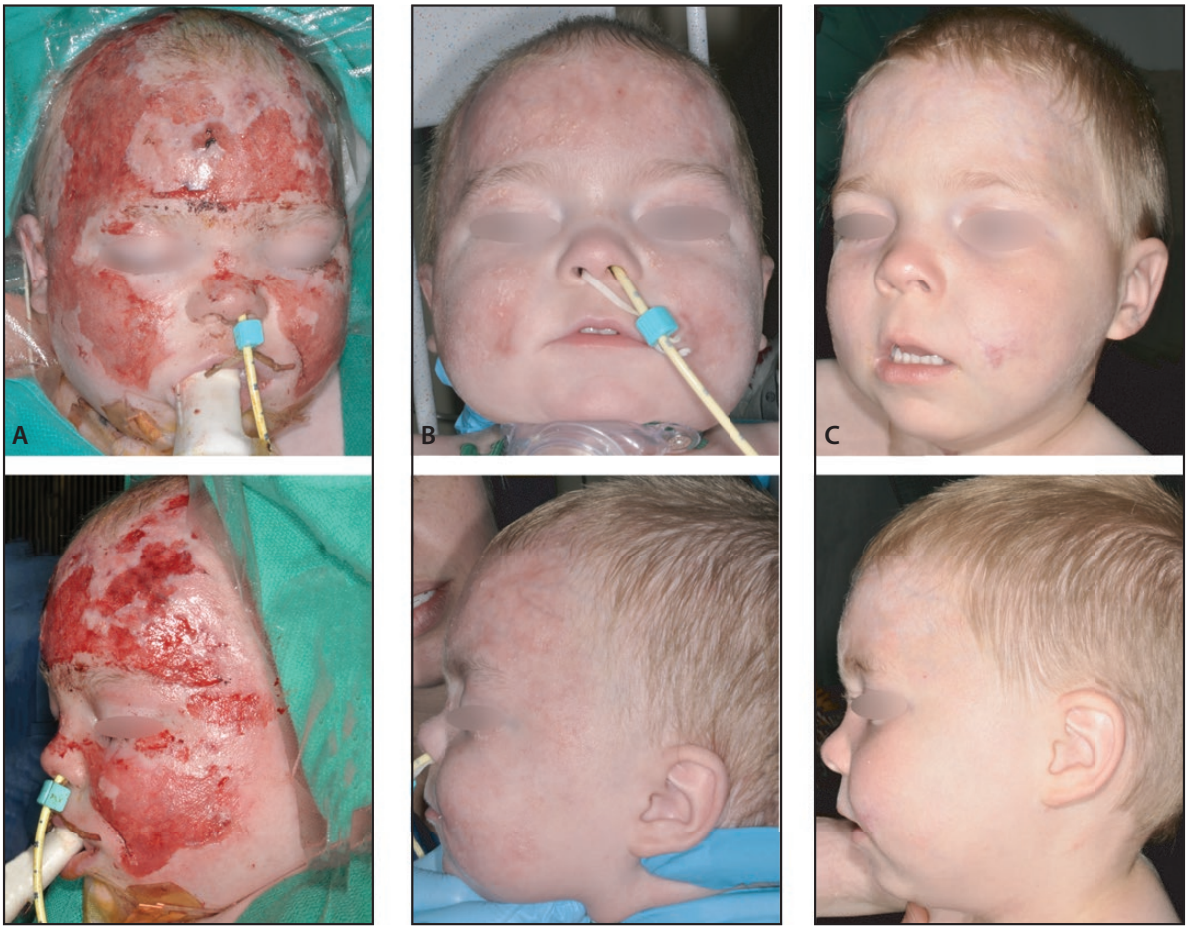

Figure 1. Two-year-old boy with a history of 35% TBSA burns who initially underwent excision and allograft 9 days after injury. (A) 29 days following initial injury, application of ASCS to facial burns. (B) 1 month after ASCS application. (C) 8 months after ASCS application.

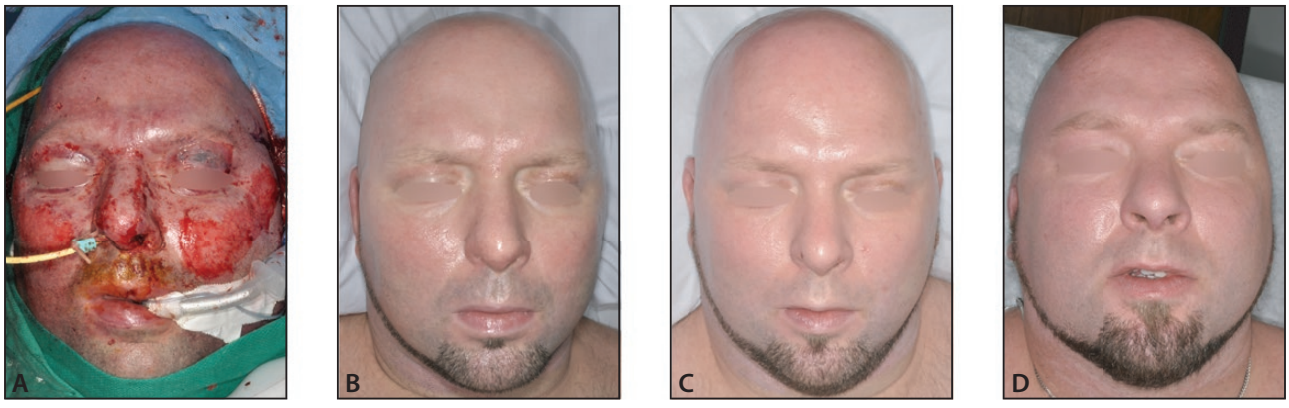

Figure 2. Forty-year-old man with a history of 52% TBSA burn who initially underwent excision and allograft 4 days after injury. (A) 24 days following initial injury, application of ASCS to facial burns. (B) 14 days after ASCS application. (C) 1 month after ASCS application. (D) 5 months after ASCS application.

burns require excision of the nonviable tissue and autografting, with or without dermal regeneration templates. Management of DPT burns can be more complex. Allowing the wounds to heal without autografting often leads to hypertrophic scarring, due to the time requirements for reepithelialization from cells found in remaining epidermal elements as well as migration from the wound margin. The usual approach of excision and autografting may result in hypertrophic scarring at the seams and dyspigmentation in the autograft itself.[8, 9] This can be particularly problematic in injuries involving the face, where aesthetic and functional outcomes are especially important. Therefore, a treatment modality that eliminates split-thickness autografting but allows for timely reepithelization would be ideal.

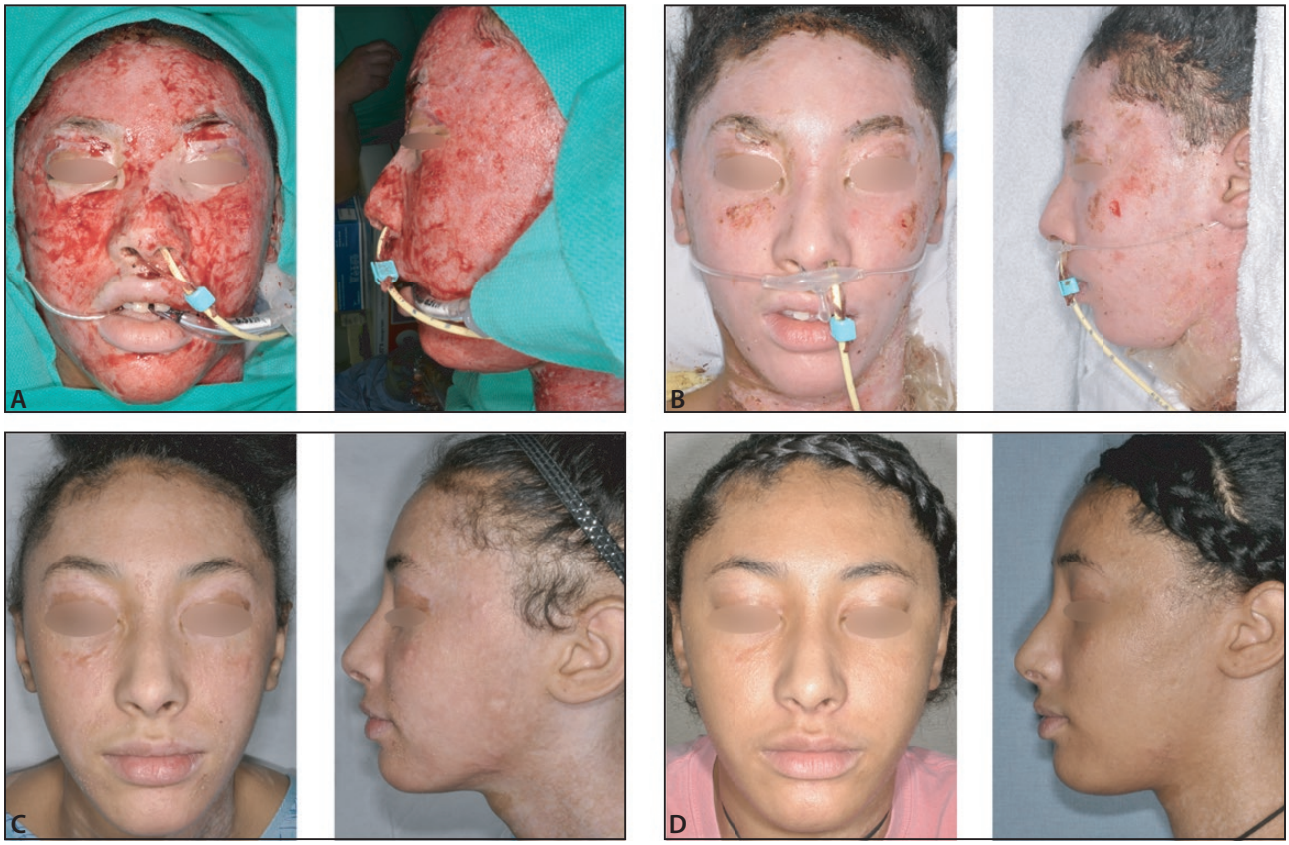

Figure 3. Twelve-year-old girl with a history of 65% TBSA burn who initially underwent excision and allograft 4 days after injury. (A) 17 days following initial injury, application of ASCS to facial burns. (B) 1 week after ASCS application. (C) 1 month after ASCS application. (D) 1 year after ASCS application.

The use of ASCS is based on the work of Wood et al, who reported that a suspension of autologous skin cells could be used for transplantation to expedite wound healing with decreased donor site size and morbidity.[3, 10, 11]The technique has been shown to deliver viable keratinocytes, melanocytes, fibroblasts, and Langerhans cells to the recipient site with resulting rapid reepithelialization, decreased adverse effects from the donor site, improved scar texture, decreased contracture rates, and improved pigmentation at the site of injury.[5, 6, 12, 13]

Successful use of ASCS in the treatment of vitiligo, chronic wounds, rhinophyma, and burn injuries of the trunk and extremities has been well-studied.[2, 11, 14–17] Studies have directly compared conventional meshed STSG with ASCS for the treatment of DPT burn injuries and have shown comparable results in time to healing and final cosmetic result, with clear benefits of ASCS over conventional STSG in terms of reduction in donor site morbidity.[6, 7, 13] However, to our knowledge, this study is first to examine the use of ASCS for DPT thermal burns of the face.

In our early experience with the application of ASCS for DPT burns, we have been able to achieve, at minimum, standard-of-care aesthetic outcomes, with several of these patients having excellent outcomes, including lack of hypertrophic scarring that is typical of conventional autografting (Figures 1 and 2). More encouraging was the excellent color match in patients of higher Fitzpatrick skin types (Figure 3). As noted by Grover and Morgan, burn injuries in this patient population can be especially difficult to treat, and STSG often leave significant color mismatch.[18] In addition, we encountered no infections or complete graft loss with over 1-year follow-up for several patients.

This study is not without its limitations. It is an observational analysis without true qualitative cosmetic evaluation such as the Vancouver Scar Scale. In addition, the determination of the depth of burn and ultimate treatment was made by a single senior author (J.A.M.). However, clinical estimation of burn depth at 1 week following the initial burn has been found in prospective studies to be accurate, when compared with more objective measurements such as laser Doppler imaging or wound biopsy.[19, 20] The designation of DPT in our study patients was further supported by the mean time from initial burn to application of ASCS of 20.6 days, as unhealed burn at 3 weeks often indicates burn depth beyond the papillary dermis and a high chance for hypertrophic scarring.[21] It is impossible to say whether our patients would have healed with similar results using standard of care excision and autografting or continued local wound care instead of ASCS. Given some of the exemplary cosmetic outcomes, our main objective for this report was to present our experience and allow readers to make their own judgments as to whether this is an appropriate technique for the treatment of DPT facial burns.

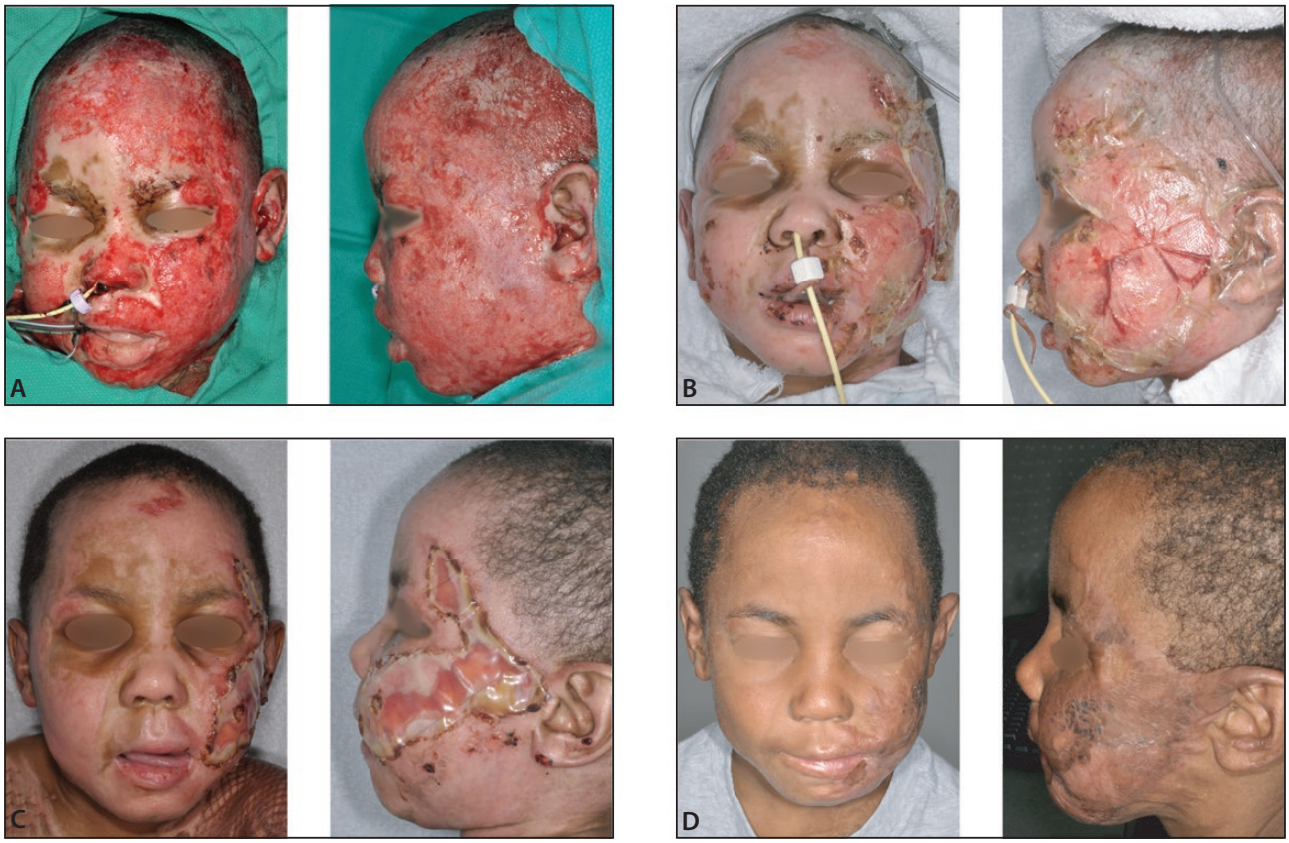

Figure 4. Four-year-old boy with a history of 49% TBSA burns who initially underwent excision and allograft 5 days after injury. (A) 12 days following initial injury, application of ASCS to facial burns. Deeper burn depth was noted at time of surgery on left cheek/lateral orbital area. (B) 1 week after ASCS application, there were obvious nonhealing areas in location of deeper burn injuries on left cheek/lateral orbital area. (C) Dermal regeneration template was applied 1 month after burn with subsequent application of epidermal autograft 2 weeks later. (D) 1 year following initial ASCS application.

Two patients in our cohort required reoperation within 3 months of applying ASCS. For one of these patients, a deeper full-thickness burn (down to subcutaneous fat) was identified on the left cheek intraoperatively, and this region eventually demonstrated poor graft take (Figure 4). With the use of ASCS, reepithelialization of the wound occurs through transplantation of in vivo proportions of skin cells, inclusive of progenitor cells, and subsequent migration, proliferation, and differentiation of the cells. However, it has been demonstrated that a viable autologous dermal component is a prerequisite for epidermal regeneration following the use of ASCS, and this is consistent with our experience.[11] One hypothesis is that the dermal layer allows for enhanced and directed angiogenesis, and the use of a dermal regeneration template in conjunction with ASCS and an autologous widely meshed skin graft has shown promising results.[22, 23] The patient did ultimately require placement of a dermal regeneration template and subsequent epidermal autografting to heal this full-thickness area of burn, resulting in typical dyspigmentation and hypertrophic scarring.

The second patient requiring reoperation within 3 months of ASCS application was a 33-year-old man who was consistently noncompliant with postoperative wound care, neck splinting, and aftercare protocols. Following excision of his burn wounds, he was initially treated with a dermal regeneration template to his neck and allograft to his face, followed by ASCS to his face and 1:1 meshed epidermal autograft with ASCS overspray to his neck. He subsequently underwent re-excision and epidermal autografting of several small, nonhealing areas on both his face and neck, to which ASCS had initially been applied. However, the major indication for reoperation was for a neck contracture release, which was directly related to his noncompliance (Figure 5). This illustrates that ASCS treatment has the same requirements for post-operative contracture management as conventional autografting. This patient also had the only complication in our case series, a superficial hematoma on postoperative day 1 (Figure 6). The decision was made not to remove the hematoma, as it was predicted that it would not negatively impact healing. The hematoma did not appear to affect healing compared to the contralateral side and was self-limiting. One proposed reason is that in the setting of direct ASCS application to a DPT with continuous dermis, a superficial hematoma bathes the cells and does not necessarily prevent imbibition as would be expected when fluid forms deep to an STSG, preventing its intimate contact with the wound bed.

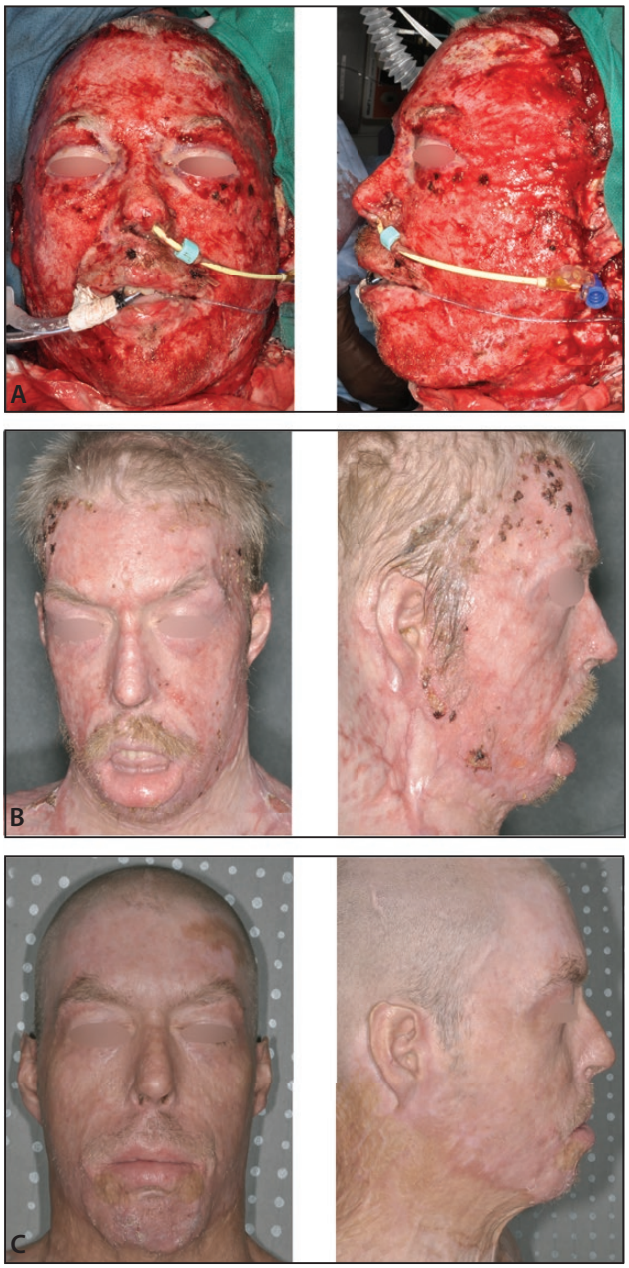

Figure 5. Thirty-three-year-old man with a history of 52% TBSA who initially underwent excision and allograft 6 days after injury. (A) 21 days following initial injury, application of ASCS to facial burns. (B) 1 month after ASCS application. (C) 1 year after ASCS application.

Further work is required to clearly define the proper patient selection for this technique. Future study designs could include patient randomization with standard of care vs ASCS using quantitative, objective evaluations for depth of burn and aesthetic outcomes.[19, 20, 24–26]

CONCLUSION

Non-cultured ASCS was used successfully to achieve definitive closure of DPT facial burns containing a confluent layer of dermis. The healing and long-term cosmetic outcomes reported demonstrate this technique warrants consideration for DPT facial burns, as traditional skin grafting and associated morbidity may be reduced.

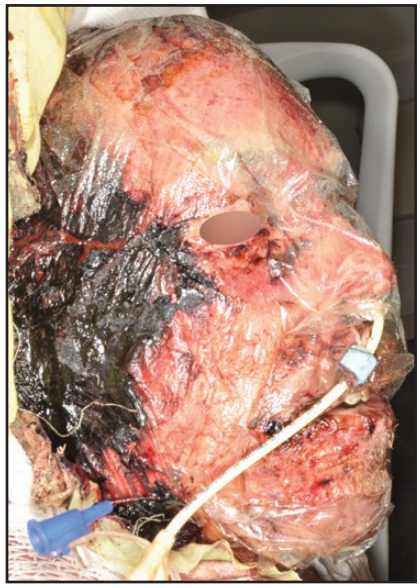

Figure 6. The previous patient (Figure 5) experienced a superficial right facial hematoma on postoperative day 1, which resolved without intervention.

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