

The Establishment of a High Standard Skin Bank in Taiwan as a Burn Care Pioneer

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Abbreviations:

NTUH: National Taiwan University Hospital; GPA: Glycerol-preserved allograft; GTP: Good Tissue Practice; TFDA: Taiwan Food and Drug Administration

1. Abstract

1.1. Introduction: The establishment of skin banks is especially important in providing crucial cadaveric skin for burn treatments. Although the 2015 Formosa Fun Coast Explosion Disaster resulted in tragic casualties, it raised public awareness of the importance of having a well-functioning skin bank and led to the initiation of a skin bank development project, as well as the establishment of the first high standard skin bank in Taiwan.

1.2. Methods: We standardized the size of our procured skin to avoid broken or disrupted skin graft, fit properly on a Zimmer Dermacarrier® for mesh expansion, and to be convenient for storage. We also integrated gamma radiation with the glycerol stored skin method for our skin preservation which effectively eradicates all contamination.

1.3. Results: From 2016 to 2020, 453,100 cm² of skin were procured from 62 donors and stored in the NTUH skin bank; 254,000 cm² of which were utilized in the treatment of 75 patients. Between 2016 and 2017, 141 microbiological examinations were administered with six were positive. Since the introduction of gamma radiation, no contamination has been observed hereafter in our examinations.

1.4. Conclusions: We report the success of establishing a high standard and well-functioning skin bank at NTUH that supply sufficient

skin allografts in Taiwan. It is the first interhospital supply of charitable skin allografts across Taiwan. Being humanitarian, our skin bank is passing great love forward.

2. Introduction

Burning trauma has always been a global threat. World Health Organization reports 180,000 annual deaths related to burn injuries [1]. Cadaveric skin plays a crucial role in treating large burn wounds. The establishment of skin banks is especially important in providing cadaveric skin for burn injury treatments with significantly improving burn survival [2, 3].

In 2015, Taiwan experienced the most severe fire catastrophe – the Formosa Fun Coast Explosion Disaster which caused 499 injuries, 281 of whom were in critical condition, and 15 died as a consequence [4]. Without a well-functioning skin bank system in Taiwan at that time, 700,000 cm² of cadaveric skin was imported by the Ministry of Health and Welfare. The incident raised public awareness of the importance of having a national skin bank, resulting in the initiation of a skin bank development project at National Taiwan University Hospital (NTUH). Armed with the mission to establish the high standard skin bank in Taiwan, Dr. HF Huang from the department of plastic surgery took on the skin bank establishment project.

A popular method used by European skin banks is the glycerol-pre-

served skin allograft (GPA) [5, 6]. High concentration of 85% glycerol was used as a storage medium. With its long-term storage temperature of 4°C, the low storage and transportation cost is one of the main advantages of the GPA. However, a disadvantage of the method is the observation of occasional contamination by the *Bacillus* bacteria [7]. Gamma-radiation has also been utilized by surgeons to decrease the contamination rate without harming the function of the skin allograft [8, 9]. With his expertise in the field, Dr. Huang integrated gamma radiation with the glycerol-preserved skin method in his establishment of the standardized skin bank at NTUH, which effectively alleviated the occurrence of *Bacillus* contamination, pioneering in skin banking in Taiwan.

3. Methods

The method used for preservation in the NTUH Skin Bank fundamentally follows the methodology of the European Skin Bank with some surgical modifications add to our protocol to improve the quality of the skin allograft [5, 10]. First, the surgical team secures the skin from the donor in the operation theater. A Zimmer Dermatome® is used to procure standardized skin pieces with each piece approximately three by seven inches (7.6 cm by 17.8 cm), with a total size of 21 in 2 (135.25 cm²). The skin then undergoes necessary trimming and experiences some degree of primary contraction, achieving a final standardized size of 15.5 in2 (100.0 cm²). The procured skin has a thickness between 0.015 to 0.020 inches (0.038 to 0.051 cm). Such procurement size effectively avoids disrupted or broken skin graft commonly seen in large-size procurement and while still fitting a Zimmer Dermacarrier® for mesh expansion properly. Another advantage of having a standardized skin area of 100 cm² is its convenience for calculation and storage in containers as the final products.

During the transportation after procurement, the skin is stored in a 50% glycerol solution at room temperature. Upon arrival at the "Good Tissue Practice" laboratory (GTP-Lab) of NTUH, the skin is then transferred into a 70% glycerol solution and undergo shaking incubation for three hours. Subsequently, the skin is transferred to an 85% glycerol solution in combination with several antibiot-

ics, including 1000 mg Streptomycin, 3 million units of Penicillin, and 50 mg Amphotericin B for three weeks. After the duration, the skin is packed in either large containers (500 cm²) or small containers (200 cm²) at the final stage.

In late 2017, we introduced the gamma radiation technique in our procured skin preservation process to tackle the challenge of contamination after storage. The GPA is treated with 15 kGy of gamma radiation after the package. Then it is refrigerated at 4°C for storage. In case of needed skin allograft, the skin would be taken out of the refrigerator, washed in 0.9% saline solution at room temperature, and used as allograft coverage of the wounds. The GPA serves as a temporary biological dressing and is widely utilized for wounds (both for full thickness and partial thickness skin loss) after the removal of non-vital tissue [11, 12], or as coverage for widely expanded autografts [13, 14]. According to the report of Hermans, we certified our GPA with two years of durability [12].

As the Formosa Fun Coast Explosion Disaster raised public awareness of the importance of a well-functioning skin bank, the Department of Plastic Surgery and the NTUH Skin Bank regularly host speeches in front of schools, public communities, and special occasions to promote skin donation. We are keeping raising the public the concept and importance of skin donation with flyers.

4. Results

4.1. Donors

From January 2016 to December 2020, there were 62 donors including 41 males and 21 females. The amount of 453,100 cm² skin was procured initially but 17,200 cm² were discarded due to positive microbiology tests either from blood culture or skin tissue culture of the donors. Finally, 435,900 cm² skin was processed and stored in the NTUH skin bank during this period. The mean age was 52.92 years in all donors with no significant difference in relation to gender. A man donated a mean of 7,648.78 cm² of procured skin and a woman 6,642.84 cm² with no significant difference ($p = 0.37$). The mean donated skin per donor was 7,308.06 cm² (Table 1). We documented the donated skin over the years in Table 2.

Table 1: Skin donors

| Category | Overall | Male | Female | p (t-test) |
|--------------------------------------|----------|----------|----------|-------------|
| Number | 62 | 41 | 21 | |
| Mean Age [year] | 52.92 | 52.47 | 53.81 | 0.86 |
| Mean Donated Size [cm ²] | 7,308.06 | 7,648.78 | 6,642.84 | 0.37 |

Table 2: Amount of donated, contaminated, stored, used and expired skin

| Year | Secured Skin [cm ²] | Initially Contaminated Skin [cm ²] | Stored Skin [cm ²] | Used Skin [cm ²] | Expired Skin [cm ²] |
|----------------|---------------------------------|--|--------------------------------|------------------------------|---------------------------------|
| 2016 | 154,700 | 11,700 | 143,000 | 21,500 | 0 |
| 2017 | 113,700 | 5,500 | 108,200 | 67,500 | 0 |
| 2018 | 47,400 | 0 | 47,400 | 75,000 | 0 |
| 2019 | 87,700 | 0 | 87,700 | 38,100 | 26,100 |
| 2020 | 49,600 | 0 | 49,600 | 51,900 | 0 |
| Overall | 453,100 | 17,200 | 435,900 | 254,000 | 26,100 |

4.2. Recipients

Between 2016 and 2020, 75 patients received procured skin as allograft treatment for various wound conditions (Figure 1). Nineteen of them received allograft treatment as a temporary biological dressing for partial-thickness burn wounds (Figure 2). Thirty-three received it for full-thickness burns after removal of non-vital tissue or overlay coverage for widely expanded autografts (Figure 3). Video S1 shows the zone of stasis of a deep burn wound after debridement on the 5th post-injury day. Immediately following the documentation of the video, we put on the cadaveric skin. Nine days later (14 days after the burn injury), the cadaveric skin was firmly engrafted on the zone and we observed healthy bright blood oozing as we were peeling off the cadaveric skin in Video S2. This sign illustrates that the prior zone of stasis has turned viable and healthy.

Three patients of toxic epidermal necrolysis received procured cadaveric skin as a temporary biological dressing. Twenty patients received skin allografts for traumatic wounds, cutaneous cancer wide excision wounds, or infected wounds after controlling microbes. During this period, the 75 recipients received a total of 254,000 cm2 of procured cadaveric skin allografts from our skin bank. It is worth mentioning that 25,500 cm2 stored skin were charitably delivered from our skin bank to other hospitals in need in Taiwan.

All the wounds regained their health in cases of the partial-thickness burn wound and toxic epidermal necrolysis. Among the 33 patients suffering from extensive full-thickness burns, five experienced resuscitation failure, and thus no engraftment occurred.

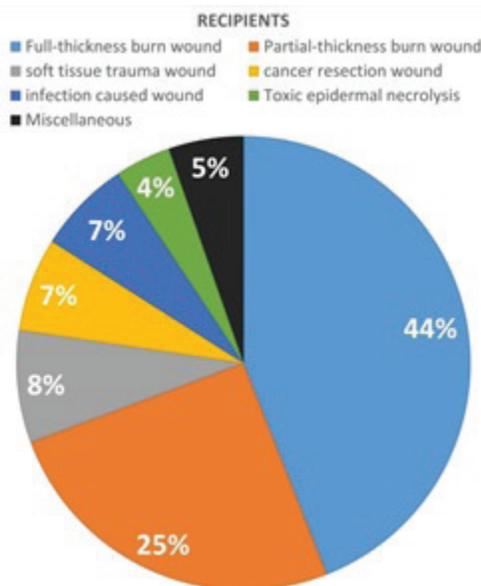


Figure 1: Recipients of different wounds with skin allografts treatment.



Figure 2: Partial-thickness burn wound (Figure 2A) with allografts treatment after 5 days (Figure 2B) and 12 days (Fig.2C).



Figure 3: Treatment of burned wound with widely meshed skin autografts and meshed skin allografts overlay.

4.3. Contamination after storage

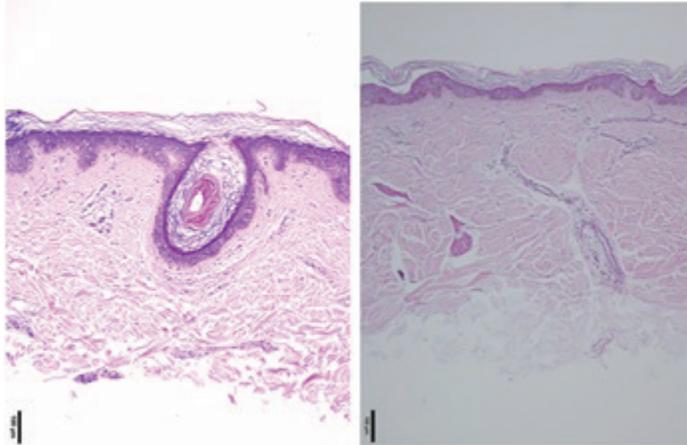
Before we put the GPA in the wounds of our patients in the operation theater, we regularly perform a microbiological examination for each container. Between 2016 and late 2017, 141 examinations were administered, among which contamination was positive in six containers, resulting in a 4.26% contamination rate. Four containers were caused by Bacillus and two containers by Paenibacillus (Table 3).

4.4. Histology study

We conduct histology tests regularly to ensure the quality and safety of our stored skin allografts. Figure 4A, 4B, 4C show that the structure of our GPA is intact and not disturbed by the glycerol process, refrigeration, and irradiation at the 6th, 12th, and 24th month tests, respectively. Meanwhile, some degree of keratolysis and nucleus shrinkage are noticeable.

Table 3: Contaminated Skin after storage

| Year of storage | Container size | Species |
|-----------------|---------------------|------------------------------|
| 2016 | 500 cm ² | <i>Bacillus subtilis</i> |
| 2016 | 500 cm ² | <i>Bacillus vallismortis</i> |
| 2016 | 500 cm ² | <i>Paenibacillus cineris</i> |
| 2016 | 500 cm ² | <i>Bacillus subtilis</i> |
| 2017 | 500 cm ² | <i>Paenibacillus cineris</i> |
| 2017 | 500 cm ² | <i>Bacillus subtilis</i> |

**Figure 4:** Histology of glycerol preserved skin allograft at 6, 12 and 24 months.(H&E stain, 20x)

5. Discussion

5.1. Method

To establish a standard skin bank, we start with skin allograft procurement. During our surgical procedure, we procure three by seven inches (7.6 cm by 17.8 cm) cadaveric skin with each piece an initial size of 21 in² (135.25 cm²) and a thickness between 0.015 to 0.020 inches (0.038 cm to 0.051 cm). To obtain a standardized final skin area of 100 cm², the procurement size is appropriate after taking the 7% primary contraction and necessary trimming into account [15]. Such procurement size effectively avoids broken or disrupted skin graft commonly seen in large-size procurement and while still fitting a Zimmer Dermacarrier® for mesh expansion properly. Another advantage of having a standardized skin area of 100 cm² is its convenience for storage in either large containers (500 cm²) or small containers (200 cm²) as well as for calculation in banking management.

We implemented the same antibiotic and antifungal treatments as in the original European Skin Bank routine. The antibiotics treating the skin allograft in the 85% glycerol solution of our preservation effectively prevent microbial contamination or proliferation, among which are streptomycin (a 30S subunit inhibitor), penicillin (beta-lactam antibiotics), and amphotericin B (an antifungal medication). The combination of the three reportedly lowers allograft discard rates [16, 17].

Our histological evaluation of the skin showed no significant decrease in skin quality as the same as the previous report [18]. Although a few skin banks show a retaining quality of the skin for up to 6 years [19], integrating our histological evaluation and the

literature, we certified our skin durability for up to 2 years [12].

5.2. Donors and Recipients

Since 2016, we received skin donations from 62 people with a total of 435,900 cm² procured skin stored in our skin bank. 254,000 cm² were utilized in the treatment of 75 patients. The well-functioning NTUH skin bank not only provides sufficient skin allograft for wounds treatment in our hospital, but it also served as the first skin allograft provider for all hospitals (interhospital supply) across the country, meeting all skin demands in Taiwan.

As the 2015 Formosa Fun Coast Explosion Disaster raised the public awareness of skin donation, we received a historically high amount of donors in 2016, with the number of organ donors increasing from 6.7 to 12.3 donors per million population. Armed with the mission to maintain such public awareness, we regularly host public speaking to propagate to the general public the fundamentals of skin donation, as well as its extensive benefits and life-saving potentials in burn treatment. Furthermore, our GPA is not only used for treating burn wounds but also provides allograft treatments extensively for other wounds due to trauma, cancers, infections, or metabolic disorders.

5.3. Contamination after storage

Bacillus plays an important role in the contamination of glycerol-stored skin. The literature shows challenges regarding *Bacillus subtilis* as it is believed that *Bacillus subtilis* could be overgrown by different flora and then be reactivated after receiving the glycerol treatment [17]. We had a similar experience that 141 examinations were administered between 2016 and 2017, among which contamination was found in six containers with all *Bacillus* spp., resulting in a 4.26% contamination rate. To tackle the contamination, gamma-radiation provides a timely solution to the contamination as it significantly lowers the infection rate without harming the function of the skin [8, 9]. We integrated gamma radiation for our GPA in late 2017, and not a single case of contamination was detected since then.

5.4. Regulations

Skin donation resembles solid organs donation in legal aspects, with its practices and procedures organized by the Taiwan Ministry of Health and Welfare in the Human Organ Transplant Act [20]. The donation can only be executed after a consent form is signed by either the donor himself/herself pre-mortem or by one's closest family member. To ensure its quality, skin procurement must be executed within 12 hours of post-mortem. The legal situation regarding laboratory work with human cells or tissue is enforced by the Taiwan Food and Drug Administration (TFDA). Good Tissue Practice (GTP) aims to raise quality standards and establish reliable quality assurance systems, as well as to prevent communicable diseases [21].

Although the 2015 Formosa Fun Coast Explosion Disaster resulted in tragic casualties, it raised public awareness of the importance of

a skin bank and a modern skin bank was born at NTUH thereafter. In addition to the establishment of a well-functioning skin bank at NTUH, Dr. HF Huang has been hosting training for practicing physicians, including skin procurement, preservation, and application training, passing down his experience to the next generations.

6. Conclusions

Today, we report the success of establishing a modern and high standard skin bank at NTUH that meets all skin demands in Taiwan. It is worth recording in Taiwan's medical history that Dr. HF Huang is the first interhospital supply of charitable skin allografts across the country. We provide contamination-free skin thanks to the integration of gamma radiation with the glycerol-stored skin method in our skin preservation. As we progress toward internationalization, we look forward to becoming an Asia skin supplier and the day when all skin demands are met.

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