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Clinical application and viability of cryopreserved cadaveric skin allografts in severe burn: A retrospective analysis

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ABSTRACT

Introduction: Cadaveric cutaneous allografts are used in burns surgery both as a temporary bio-dressing and occasionally as definitive management of partial thickness burns. Nonetheless, limitations in the understanding of the biology of these grafts have meant that their role in burns surgery continues to be controversial.

Methods: A review of all patients suffering 20% or greater total body surface area (TBSA) burns over an eight year period that received cadaveric allografts were identified. To investigate whether tissue viability plays a role in engraftment success, five samples of cryopreserved cadaveric cutaneous allograft processed at the Donor Tissue Bank of Victoria (DTBV) were submitted to our laboratory for viability analysis using two methods of Trypan Blue Exclusion and tetrazolium salt (MTT) assays.

Results: During the study period, 36 patients received cadaveric allograft at our institution. The average total burn surface area (TBSA) for this group of patients was 40% and all patients received cadaveric skin as a temporizing measure prior to definitive grafting. Cadaveric allograft was used in complicated cases such as wound contamination, where synthetic dressings had failed. Viability tests showed fewer than 30% viability in processed allografts when compared to fresh skin following the thawing process. However, the skin structure in the frozen allografts was histologically well preserved.

Conclusion: Cryopreserved cutaneous cadaveric allograft has a positive and definite role as an adjunct to conventional dressing and grafting where available, particularly in patients with large TBSA burns. The low viability of cryopreserved specimens processed at DTBV suggests that cell viability in cadaveric allograft may not be essential for its clinical function as a wound dressing or even as permanent dermal substitute.

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1. Introduction

Human cadaveric cutaneous allograft has been used in the management of burns for over 50 years [1]. During this time, clinical, technological, medico-legal and tissue banking developments have changed the context in which clinicians manage severely injured burn patients. Burns units have evolved their own treatment algorithms which are largely dependent on local resources and clinician preference. This is especially true with respect to wound management practices in those with massive burns.

Despite the availability of various kinds of skin substitutes for clinical and research use, autologous skin grafting remains the primary treatment of choice for deep burns, and indeed if a patient with extensive deep burns is to survive, burns must be grafted eventually with autologous skin. When this is not initially feasible, due to limited donor sites or host wound bed factors, there is a requirement for alternative methods of wound closure. Tissue engineered skin substitutes are currently available for use in uncontaminated wounds, and can adhere and provide wound closure pending availability of autologous grafts; however, they can be highly demanding of technical expertise for production and in the requirement for meticulous wound bed preparation and after application management practices for successful engraftment.

Cadaveric allograft may also be applied to the burn wound as a temporizing measure [2–4]. In addition, cadaveric allografts have been advocated by some authors as a definitive dressing for partial thickness burns and as wound bed preparation after excision of full thickness burns [3]. In contrast to available synthetic skin substitutes, allograft possesses many of the desirable properties of autologous skin. In particular, it has the ability to adhere to and engraft a suboptimal host wound bed, taking a blood supply and providing wound closure until host rejection of the cellular elements. This results in wound closure which promotes retention of moisture and electrolytes and improved thermoregulation [5,6]. In addition, allografts decrease wound pain, lower bacterial loads in contaminated wounds, and may provide dermal matrix elements which can persist [7,8] and improve final graft properties and scarring after definitive autografting.

Two common methods of preserving cadaveric allografts are in use by tissue banks: cryopreservation and 85% glycerol preservation, and there is ongoing debate regarding the relative clinical merits of glycerol preserved and cryopreserved allograft [9,10]. In comparison to cryopreserved skin, 85% glycerol preservation has antibacterial and antiviral effect [11,12], and allows for more cost efficient long term storage and ease of distribution. However it results in essentially unviable skin, which may be associated with decreased clinical utility [13,14]. The current role of allograft skin in the management of burn varies between burn units, many of which do not have access to or experience with use of this product. In addition, developments in the medico-legal environments in which clinicians and tissue banks operate have increased resource requirements for compliance with various standards. The value of and indications for allograft skin for management of burns patients, and the cost–benefit ratio of different methods of skin tissue banking are not issues on which there is universal agreement. The DTBV is the only fully operational multi tissue bank (skin, musculoskeletal and cardiac tissue) facility in Australia. It developed a skin banking program in 1994 [14]. The Victorian Adult Burns Service (VABS) at the Alfred Hospital is the state-wide provider of burns care for all adults with complex or major burns, serving a population of 5.5 million in south-eastern Australia.

The supply of cadaveric skin allograft is extremely limited in Australia. This paper presents our unit's current algorithm for management of patients with severe burn. The results of analysis of the properties of cryopreserved skin produced by the DTBV are presented, and the indications for use of this skin are discussed in the light of our findings and current logistical realities.

2. Materials and methods

2.1. *Clinical material*

Allograft is used as a temporary method of sealing and stabilizing deep excised burn wounds prior to definitive grafting with autologous split skin graft. Our current management algorithm reserves allograft for use in patients with large burns in whom synthetic or composite skin substitutes have failed (Fig. 1). This is in part due to limited availability of allograft. If stocks allow, allograft is also used for wound closure over widely meshed autograft [15]. Allograft routinely adheres to excised and contaminated burn wounds. The dermis can persist for at least some weeks in a wound bed (Fig. 2), and allograft dermis is not routinely removed prior to autografting. If allograft epidermal elements are present at the time of autografting, these are removed using hydrosurgical excision (Versajet™) prior to grafting. In partial thickness wounds, allograft supports re-epithelialization (Fig. 3). After institutional ethics approval, patients with greater than 20% TBSA burns admitted to the hospital during an 8 year period (January 2002–January 2010) were identified using the Alfred Hospital's VABS database. A chart review of these patients was undertaken and patients receiving cadaveric allograft were identified.

2.2. *Cryopreservation*

Skin tissue is retrieved within 24 h of death and exposed to antibiotics for a minimum of 12 h. The skin is exposed to a cryopreservation bath (cell culture media + DMSO), and packaged in double, freeze resistant, plastic and aluminum pouches. Samples for microbiological monitoring are removed at different stages during this process. The skin is frozen to −40 °C at a rate of 1°/min, and stored in quarantine in liquid nitrogen. Tissues are released for clinical use only after the final quality review, which includes all processing data and information contained in the donor file.

2.3. *Viability assays*

Cryopreserved skin tissues (I–V) processed at the DTBV, donated from five individuals with an age range of 42–63